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FILE 'HOME' ENTERED AT 12:44:11 ON 19 APR 2002

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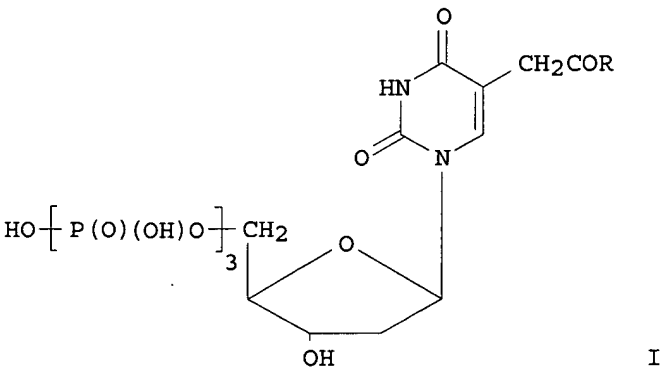
L4 ANSWER 1 OF 36 CA COPYRIGHT 2002 ACS
ACCESSION NUMBER: 136:263388 CA
TITLE: Nucleic acid synthesis using new 5-substituted deoxyuridine derivatives by PCR with superthermophilic DNA polymerase
INVENTOR(S): Sawai, Hiroaki; Ozaki, Akiko; Masud, Mohammad M.; Sato, Fumie; Ozaki, Hiroaki
PATENT ASSIGNEE(S): Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 17 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2002085079	A2	20020326	JP 2000-282430	20000918

GI



I

AB A method of nucleic acid synthesis using new 5-substituted deoxyuridine derivs. I (R = OX or NHY, X = H, alkyl, alkenyl, alkynyl, or aryl, Y = H, alkyl, alkenyl, alkynyl, aryl, (CH2)n, or NHZ, (CH2)2N[(CH2)2NHZ]2, Z = H, COCF3, COCH3, carboxy Me imidazole, histidyl, aspargyl, or glutamyl, n = 2, 3, 4, or 6) as substrates by PCR with superthermophilic DNA polymerase, is disclosed. The method is based on the discovery that certain DNA polymerases, KOD Dash DNA polymerase or KOD DNA polymerase, in particular, can use those 5-substituted deoxyuridine derivs., obtained by the reaction of arabino amino-oxazoline and .alpha.-bromomethyl fumarate, as substrates, unlike other DNA polymerases. KOD Dash DNA polymerase can accept triphosphates of new deoxyuridine derivs. bearing a C5-substituent group via an .alpha.-methylene linker as a substrate in the polymerase chain reaction (PCR) yielding the corresponding functionalized DNA effectively, while other conventional DNA polymerases cannot tolerate the modification of the substrate. Novel thymidine analog triphosphates,

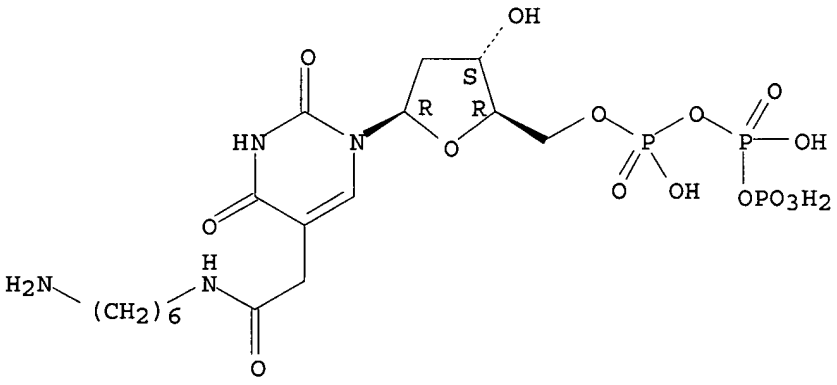
which have an sp3-hybridized carbon at the C5 .alpha.-position with amino-linker arms, a Me ester, or a carboxyl group at the C5 sidearm, were good substrates for primer-extension reactions by DNA polymerase from Pyrococcus kodakaraensis (KOD Dash DNA polymerase), yielding exclusively full-length products. The resulting modified DNA was further allowed to react with a functional mol. such as fluorescein isothiocyanate. By contrast, only truncated products were formed from the thymidine analog substrate bearing the amino-linker arm or the neg. charged carboxyl group using Taq, Tth DNA polymerase, or DNA polymerase I from E. coli (Klenow fragment). The results indicate either that the thymidine analog was not accepted by the enzymes, or that the polymerases could not extend the products, once the analog had been incorporated, depending on the type of the analog. A conventional thymidine analog bearing an aminopropenyl group at the C5-position was accepted by all enzymes, among which KOD Dash DNA polymerase showed the highest activity for the polymn. with this analog. Templates bearing the thymidine analogs in place of one thymidine residue were read by KOD Dash, Taq, Tth DNA polymerases, and the Klenow fragment giving the full-length product. KOD Dash DNA polymerase could expand structural diversities of substrates that can be used to prep. modified DNAs.

IT **402789-71-3**
RL: BCP (Biochemical process); RCT (Reactant); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent)
(nucleic acid synthesis using new 5-substituted deoxyuridine derivs. by PCR with superthermophilic DNA polymerase)

RN 402789-71-3 CA

CN Uridine 5'-(tetrahydrogen triphosphate), 5-[2-[(6-aminohexyl)amino]-2-oxoethyl]-2'-deoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **402789-71-3 402789-73-5 402789-74-6**
RL: BCP (Biochemical process); RCT (Reactant); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent)
(nucleic acid synthesis using new 5-substituted deoxyuridine derivs. by PCR with superthermophilic DNA polymerase)

L4 ANSWER 2 OF 36 CA COPYRIGHT 2002 ACS
ACCESSION NUMBER: 136:263105 CA
TITLE: Octahydroindolizine and quinolizine and hexahydropyrrolizine derivatives as histaminic H1 and H3 antagonists
INVENTOR(S): Apodaca, Richard; Carruthers, Nicholas I.; Carson, John R.; Chai, Wenying; Kwok, Annette K.; Li,

Xiaobing; Lovenberg, Timothy W.; Rudolph, Dale A.; Shah, Chandravadan R.
PATENT ASSIGNEE(S): Ortho McNeil Pharmaceutical, Inc., USA
SOURCE: PCT Int. Appl., 164 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002024695	A2	20020328	WO 2001-US29624	20010921

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-234504P P 20000922
US 2000-234505P P 20000922

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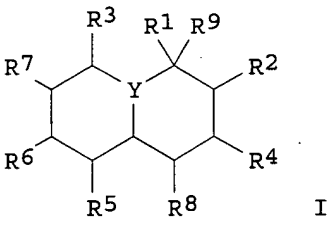

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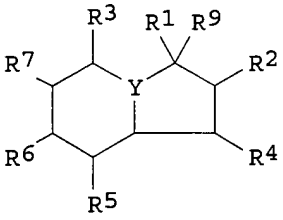

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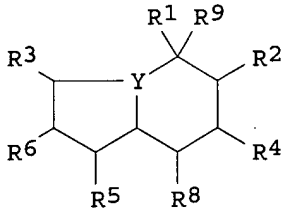

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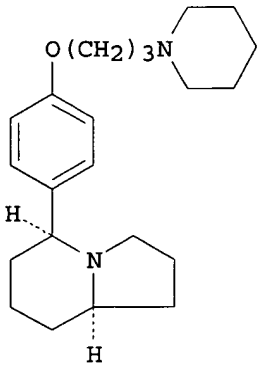


IV

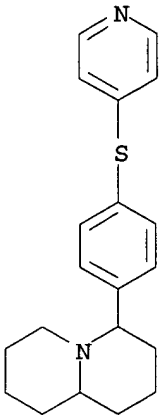
AB Title compds. I-III [Y = N, N=O; one of R1-R3 = substituted cycloalkyl, Ph, naphthyl, heterocyclyl, cycloalkylalkyl, phenylalkyl, naphthylalkyl, heterocyclylalkyl, the others are H, halogen, alkyl; R4, R5, R7, R8 = H, halogen, alkyl, alkoxy; R6 = H, O, Ph; R9 = H, CN, alkyl, alkylamino] were prepd. for use as histaminic H1 and H3 antagonists in treatment of **histamine**-mediated diseases and conditions. Thus, the indolizine

IV was prepd. by reaction of 4-H2N(CH2)3CH(OMe)2 with OC(CH2CO2Et)2 and 4-MeOC6H4CHO to give 5-(4-methoxyphenyl)-7(8H)-indolizinone, redn. of the oxo group, demethylation, and reaction with 1-(3-chloropropyl)piperidine. IV had a Ki of 0.7 nM for N-methylhistamine binding.

IT **405314-40-1P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of octahydroindolizine and quinolizine and hexahydropyrrolizine derivs. as histaminic H1 and H3 antagonists)

RN 405314-40-1 CA

CN 2H-Quinolizine, octahydro-4-[4-(4-pyridinylthio)phenyl]- (9CI) (CA INDEX NAME)



IT **405314-40-1P 405314-42-3P 405314-46-7P**
405314-52-5P 405314-53-6P 405314-62-7P
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405314-82-1P 405314-86-5P 405314-89-8P
405314-90-1P 405314-94-5P 405314-97-8P
405314-98-9P 405315-00-6P 405315-07-3P
405315-12-0P 405315-13-1P 405315-14-2P
405315-17-5P 405315-19-7P 405315-20-0P
405315-21-1P 405315-24-4P 405315-25-5P
405315-28-8P 405315-30-2P 405315-31-3P
405315-34-6P 405315-35-7P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of octahydroindolizine and quinolizine and hexahydropyrrolizine derivs. as histaminic H1 and H3 antagonists)

IT **405314-28-5P 405314-29-6P 405314-30-9P**
405314-31-0P 405314-32-1P 405314-33-2P
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405314-37-6P 405314-38-7P 405314-39-8P
405314-41-2P 405314-43-4P 405314-44-5P
405314-45-6P 405314-47-8P 405314-48-9P
405314-49-0P 405314-50-3P 405314-51-4P
405314-54-7P 405314-55-8P 405314-56-9P
405314-57-0P 405314-58-1P 405314-59-2P
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405315-57-3P 405315-71-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of octahydroindolizine and quinolizine and hexahydropyrrolizine derivs. as histaminic H1 and H3 antagonists)

IT **398473-98-8P 405314-79-6P 405314-92-3P**
405314-93-4P 405315-50-6P 405315-51-7P
405315-52-8P 405315-53-9P 405315-54-0P
405315-55-1P 405315-56-2P 405315-58-4P
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405315-62-0P 405315-63-1P 405315-64-2P
405315-65-3P 405315-66-4P 405315-67-5P
405315-68-6P 405315-69-7P 405315-70-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of octahydroindolizine and quinolizine and hexahydropyrrolizine derivs. as histaminic H1 and H3 antagonists)

IT **405315-75-5P 405315-76-6P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of octahydroindolizine and quinolizine and hexahydropyrrolizine derivs. as histaminic H1 and H3 antagonists)

L4 ANSWER 3 OF 36 CA COPYRIGHT 2002 ACS
ACCESSION NUMBER: 136:263087 CA
TITLE: Preparation of 1,3-di- and 1,3,3-trisubstituted pyrrolidines as **histamine**-3 receptor ligands for treatment of Alzheimer's disease, ADHD, epilepsy, and narcolepsy
INVENTOR(S): Bennani, Youssef L.; Faghih, Ramin; Dwight, Wesley J.; Vasudevan, Anil; Conner, Scott E.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 54 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002035103	A1	20020321	US 2001-902925	20010711

PRIORITY APPLN. INFO.: US 2000-218084P P 20000713

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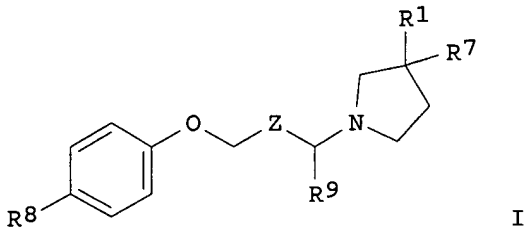

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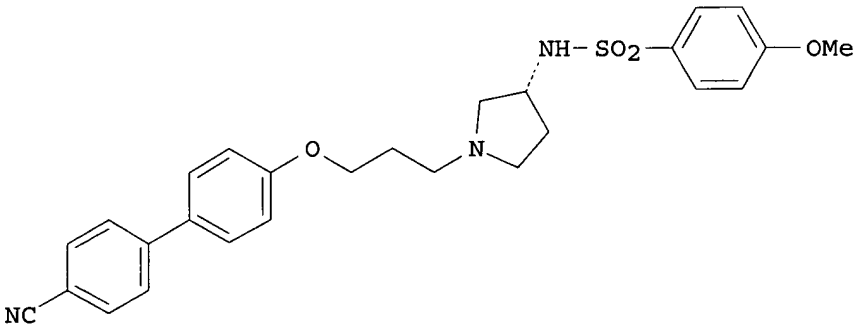


II

AB Title compds. I [wherein Z = a bond or CH2; R1 = OR2, NR3R4, or substituted 2,5-dioxoimidazolidinyl; R2 = H, alkoxycarbonyl, alkyl(carbonyl), aminocarbonyl, sulfono, or phosphono; R3 and R4 = independently H, alkenyl(sulfonyl), alkenyl(oxy)carbonyl, alkoxycarbonyl, alkyl(sulfonyl), alkylcarbonyl, aminocarbonyl, aminosulfonyl, alkynyl(sulfonyl), alkynyl(oxy)carbonyl, or (un)substituted (hetero)arylalkyl, (hetero)arylalkenylcarbonyl, etc.; R7 = H or alkyl; or R1 and R7 together form :O; R8 = (cyclo)alkylcarbonyl, or (un)substituted aryl(carbonyl), arylcarbonylaryl, arylcarbonylheterocyclyl, cycloalkylcarbonylaryl, cycloalkylcarbonylheterocyclyl, heterocyclyl(carbonyl), heterocyclylcarbonylaryl, or heterocyclylcarbonylheterocyclyl; R9 = H or alkyl] were prepd. as **histamine**-3 receptor ligands. For example, 4'-[3-[(3R)-3-aminopyrrolidinyl]propoxy][1,1'-biphenyl]-4-carbonitrile in CH2Cl2 was treated with polymer supported N,N-diisopropylethylamine, catalytic N,N-dimethylaminopyridine, and 4-methoxybenzenesulfonyl chloride. After shaking at ambient temp. for 14 h, the mixt. was treated with tris(2-aminoethyl)amine-polystyrene resin and the mixt. shaken for an addnl. 2 h to give the [[(biphenylyloxy)propyl]pyrrolidinyl]benzenesulfonamide II (79%). The latter bound to the **histamine**-3 receptor with Ki of 12 nM. I are useful for the treatment of acute myocardial infarction, asthma, cutaneous carcinoma, depression, inflammation, medullary thyroid carcinoma, melanoma, Meniere's disease, migraine, motion sickness, obesity, pain, Parkinson's disease, schizophrenia, seizures, septic shock, Alzheimer's disease, attention-deficit hyperactivity disorder (ADHD), epilepsy, and narcolepsy.

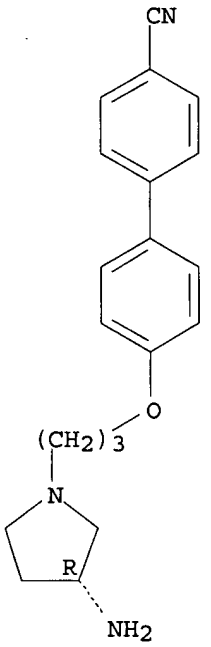
IT **392337-21-2P**, 4'-[3-((3R)-3-Aminopyrrolidinyl)propoxy][1,1'-biphenyl]-4-carbonitrile

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(**histamine**-3 receptor ligand; prepn. of di- and trisubstituted pyrrolidines as **histamine**-3 receptor ligands for treatment of Alzheimer's disease, ADHD, epilepsy, and narcolepsy)

RN 392337-21-2 CA

CN [1,1'-Biphenyl]-4-carbonitrile, 4'-[3-[(3R)-3-amino-1-pyrrolidinyl]propoxy]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **392337-21-2P**, 4'-[3-((3R)-3-Aminopyrrolidinyl)propoxy][1,1'-biphenyl]-4-carbonitrile **392338-14-6P 392338-16-8P 392338-59-9P 392338-60-2P**, 4'-[3-(3-Oxo-1-pyrrolidinyl)propoxy][1,1'-biphenyl]-4-carbonitrile
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(**histamine**-3 receptor ligand; prepn. of di- and trisubstituted pyrrolidines as **histamine**-3 receptor ligands for treatment of Alzheimer's disease, ADHD, epilepsy, and narcolepsy)

IT **392337-05-2P 392337-07-4P 392337-08-5P 392337-09-6P**, N-[(3R)-1-[3-(4-Acetylphenoxy)propyl]pyrrolidinyl]-2-(3-pyridinyl)-1,3-thiazole-4-carboxamide **392337-10-9P 392337-11-0P**, N-[(3R)-1-[3-(4-Acetylphenoxy)propyl]pyrrolidinyl]-2-propanesulfonamide **392337-12-1P 392337-13-2P 392337-14-3P**, (5S)-3-[(3R)-1-[3-(4-Acetylphenoxy)propyl]pyrrolidinyl]-5-methyl-2,4-imidazolidinedione **392337-15-4P 392337-16-5P**, 4-Cyano-N-[(3R)-1-[3-[4-(cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]benzenesulfonamide **392337-17-6P 392337-18-7P 392337-19-8P**, N-[(3R)-1-[3-(4-Acetylphenoxy)propyl]pyrrolidinyl]-4-cyanobenzamide **392337-20-1P 392337-22-3P 392337-23-4P 392337-24-5P 392337-25-6P 392337-26-7P**,

N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-4-methoxybenzenesulfonamide **392337-27-8P 392337-28-9P 392337-29-0P 392337-30-3P 392337-31-4P**, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-2-methylbenzenesulfonamide **392337-32-5P**, 3-Chloro-N-[(3R)-1-[3-[(4'-cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-4-fluorobenzenesulfonamide **392337-33-6P 392337-34-7P 392337-35-8P 392337-36-9P 392337-37-0P**, 3-Chloro-N-[(3R)-1-[3-[(4'-cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]benzenesulfonamide **392337-38-1P 392337-39-2P 392337-40-5P 392337-41-6P 392337-42-7P**, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-2-thiophenesulfonamide **392337-43-8P 392337-44-9P 392337-45-0P 392337-46-1P 392337-47-2P**, 4-Butoxy-N-[(3R)-1-[3-[(4'-cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]benzenesulfonamide **392337-48-3P 392337-49-4P 392337-50-7P**, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-2-phenylethenesulfonamide **392337-51-8P 392337-52-9P 392337-53-0P**, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-3-methylbenzenesulfonamide **392337-54-1P 392337-55-2P**, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-2,4-difluorobenzenesulfonamide **392337-56-3P 392337-57-4P 392337-58-5P**, 3,4-Dichloro-N-[(3R)-1-[3-[(4'-cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]benzenesulfonamide **392337-59-6P 392337-60-9P**, 4-Bromo-N-[(3R)-1-[3-[4-(cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]benzenesulfonamide **392337-61-0P 392337-62-1P 392337-63-2P**, N-[(3R)-1-[3-[4-(Cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]-4-methoxybenzenesulfonamide **392337-64-3P**, 4-tert-Butyl-N-[(3R)-1-[3-[4-(cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]benzenesulfonamide **392337-65-4P**, N-[(3R)-1-[3-[4-(Cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]-4-methylbenzenesulfonamide **392337-66-5P 392337-67-6P 392337-68-7P 392337-69-8P**, 3-Chloro-N-[(3R)-1-[3-[4-(cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]-4-fluorobenzenesulfonamide **392337-70-1P**, N-[(3R)-1-[3-[4-(Cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]-4-ethylbenzenesulfonamide **392337-71-2P 392337-72-3P 392337-73-4P 392337-74-5P**, 3-Chloro-N-[(3R)-1-[3-[4-(cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]benzenesulfonamide **392337-75-6P**, 3-Cyano-N-[(3R)-1-[3-[4-(cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]benzenesulfonamide **392337-76-7P**, N-[(3R)-1-[3-(4-Acetylphenoxy)propyl]pyrrolidinyl]-3-fluorobenzenesulfonamide **392337-77-8P 392337-78-9P 392337-79-0P**, N-[(3R)-1-[3-(4-Acetylphenoxy)propyl]pyrrolidinyl]-5-isoquinolinesulfonamide **392337-80-3P 392337-81-4P**, N-[(3R)-1-[3-(4-Acetylphenoxy)propyl]pyrrolidinyl]-3,4-dichlorobenzenesulfonamide **392337-82-5P 392337-84-7P**, N-[(3R)-1-[3-(4-Acetylphenoxy)propyl]pyrrolidinyl]-4-[[3-chloro-5-(trifluoromethyl)-2-pyridinyl]oxy]benzenesulfonamide **392337-85-8P 392337-86-9P**, N-[(3R)-1-[3-[4-(Cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]-2-thiophenesulfonamide **392337-87-0P 392337-88-1P 392337-89-2P**, N-[(3R)-1-[3-[4-(Cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]-8-quinolinesulfonamide **392337-90-5P 392337-92-7P 392337-93-8P 392337-94-9P**, N-[(3R)-1-[3-[4-(Cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]-2-phenylethenesulfonamide **392337-95-0P 392337-96-1P**, 2-Cyano-N-[(3R)-1-[3-[4-(cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]benzenesulfonamide **392337-97-2P 392337-98-3P 392337-99-4P**

392338-00-0P 392338-01-1P 392338-02-2P,
3,4-Dichloro-N-[(3R)-1-[3-[4-(cyclopropylcarbonyl)phenoxy]propyl]pyrrolidinyl]benzenesulfonamide **392338-03-3P 392338-04-4P**
392338-05-5P 392338-06-6P 392338-08-8P
392338-09-9P 392338-10-2P 392338-11-3P
392338-12-4P, N-[2-Chloro-4-[[[(3R)-1-[3-[4-(2-pyridinyl)phenoxy]propyl]pyrrolidinyl]amino]sulfonyl]phenyl]acetamide
392338-13-5P, 4'-[3-[(3R)-3-(Dimethylamino)pyrrolidinyl]propoxy][1,1'-biphenyl]-4-carbonitrile **392338-17-9P 392338-18-0P**
, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-N,3,3-trimethylbutanamide **392338-19-1P 392338-20-4P**
392338-21-5P 392338-22-6P 392338-23-7P,
N'-tert-Butyl-N-[(3R)-1-[3-[[4'-cyano(,1'-biphenyl)-4-yl]oxy]propyl]pyrrolidinyl]-N-methylurea **392338-24-8P**
392338-25-9P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-4-fluoro-N-methylbenzamide
392338-26-0P 392338-27-1P 392338-28-2P,
N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-N-methyl-2-furamide **392338-29-3P 392338-30-6P**,
N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-N,N',N'-trimethylsulfamide **392338-31-7P 392338-32-8P**
392338-33-9P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-4-isopropyl-N-methylbenzenesulfonamide
392338-34-0P 392338-35-1P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-4-fluoro-N-(4-fluorobenzoyl)benzamide **392338-36-2P 392338-37-3P**
392338-38-4P, Allyl (3R)-1-[3-[(4'-cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinylcarbamate **392338-39-5P**, Methyl (3R)-1-[3-[(4'-cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinylcarbamate
392338-40-8P, tert-Pentyl (3R)-1-[3-[(4'-cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinylcarbamate **392338-41-9P**
392338-42-0P 392338-43-1P 392338-44-2P,
N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-4-morpholinecarboxamide **392338-45-3P**, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-4-fluorobenzamide
392338-46-4P 392338-47-5P 392338-48-6P
392338-49-7P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-2-(3-pyridinyl)-1,3-thiazole-4-carboxamide
392338-50-0P 392338-51-1P, N'-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-N,N-dimethylsulfamide
392338-52-2P 392338-53-3P 392338-54-4P
392338-55-5P 392338-56-6P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-N-(4-morpholinylcarbonyl)-4-morpholinecarboxamide **392338-57-7P 392338-58-8P**,
Cyclopropyl[4-[3-((3R)-3-hydroxypyrrolidinyl)propoxy]phenyl]methanone
392338-61-3P, 4'-[3-((3S)-3-Hydroxypyrrolidinyl)propoxy][1,1'-biphenyl]-4-carbonitrile **392338-62-4P**, 4'-[3-(3-Hydroxy-3-methyl-1-pyrrolidinyl)propoxy][1,1'-biphenyl]-4-carbonitrile **392338-63-5P**
, 4'-[3-(3-Hydroxy-3-isopropyl-1-pyrrolidinyl)propoxy][1,1'-biphenyl]-4-carbonitrile **392338-64-6P**, 4'-[3-((3R)-3-Hydroxy-3-methylpyrrolidinyl)propoxy][1,1'-biphenyl]-4-carbonitrile
392338-66-8P 392338-67-9P, N,N-Dimethyl-N-[(3S)-1-[3-[[4'-(1-pyrrolidinylcarbonyl)[1,1'-biphenyl]-4-yl]oxy]propyl]pyrrolidinyl]amine **392338-68-0P**
392338-69-1P 392338-71-5P 392338-72-6P,
N-[(3R)-1-[3-[[4'-Cyano(,1'-biphenyl)-4-yl]oxy]propyl]pyrrolidinyl]-3-fluorobenzenesulfonamide **392338-73-7P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(**histamine**-3 receptor ligand; prepn. of di- and trisubstituted pyrrolidines as **histamine**-3 receptor ligands for treatment of Alzheimer's disease, ADHD, epilepsy, and narcolepsy)

IT **392337-06-3P**, 1-[4-[3-[(3R)-3-Aminopyrrolidinyl]propoxy]phenyl]ethanone **392338-07-7P**, (3R)-1-[3-[4-(2-Pyridinyl)phenoxy]propyl]pyrrolidinylamine
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of di- and trisubstituted pyrrolidines as **histamine**-3 receptor ligands for treatment of Alzheimer's disease, ADHD, epilepsy, and narcolepsy)

IT **392337-91-6**, [4-[3-((3R)-3-Aminopyrrolidinyl)propoxy]phenyl](cyclopropyl)methanone **392338-15-7**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; prepn. of di- and trisubstituted pyrrolidines as **histamine**-3 receptor ligands for treatment of Alzheimer's disease, ADHD, epilepsy, and narcolepsy)

L4 ANSWER 4 OF 36 CA COPYRIGHT 2002 ACS
ACCESSION NUMBER: 136:260531 CA
TITLE: Rat and human genes for a novel mammalian biogenic amine receptor and their use in the development of therapeutics
INVENTOR(S): Bunzow, James R.; Grandy, David K.; Sonders, Mark
PATENT ASSIGNEE(S): Oregon Health & Science University, USA
SOURCE: PCT Int. Appl., 86 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002022801	A2	20020321	WO 2001-US28455	20010912

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

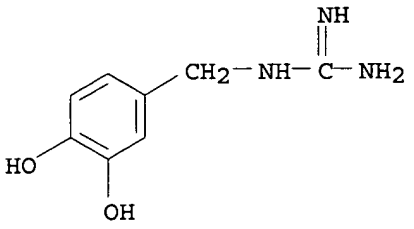
PRIORITY APPLN. INFO.: US 2000-659519 A1 20000912
US 2001-303967P P 20010709

AB The present invention relates to novel mammalian biogenic amine receptor proteins and genes that encode such proteins. The invention is directed toward the isolation and characterization of mammalian trace amine receptor proteins. The invention specifically provides isolated complementary DNA copies of mRNA corresponding to rat and human homologues of a mammalian trace amine receptor gene. Also provided are recombinant expression constructs capable of expressing the mammalian trace amine receptor genes of the invention in cultures of transformed prokaryotic and eukaryotic cells, as well as such cultures of transformed cells that synthesize the mammalian trace amine receptor proteins encoded therein. The invention also provides methods for screening compds. in vitro that are capable of binding to the mammalian trace amine receptor proteins of the invention, and further characterizing the binding properties of such compds. and functional consequences thereof in comparison with known trace

amine receptor agonists and antagonists. Improved methods of pharmacol. screening are provided thereby. The rat gene was identified by cloning G protein-coupled receptor cDNAs by RT-PCR using degenerate primers. The primary clone was used as a probe to screen a genomic library for a full-length gene. A sequence showing similarities to dopaminergic, adrenergic, serotoninergic and **histaminergic** receptors was obtained. Distribution of the mRNA was consistent known patterns of distribution of trace amine receptors. Cloning and mapping of the corresponding human gene is described. Use of a reporter gene system to analyze the pharmacol. of the rat receptor is demonstrated. The method places a green fluorescent protein gene under control of the G protein-coupled receptor-activated MAP kinase pathway. Activation of the pathway by a no. of ligands is demonstrated. The pharmacol. of the receptor did not correspond to that of any known biogenic amine receptor.

IT **404887-82-7**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(as agonist of biogenic amine receptor; rat and human genes for novel mammalian biogenic amine receptor and their use in development of therapeutics)

RN 404887-82-7 CA
CN INDEX NAME NOT YET ASSIGNED



IT **404887-82-7**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(as agonist of biogenic amine receptor; rat and human genes for novel mammalian biogenic amine receptor and their use in development of therapeutics)

L4 ANSWER 5 OF 36 CA COPYRIGHT 2002 ACS
ACCESSION NUMBER: 136:247498 CA
TITLE: Acylaminoalkylpiperidines as chemokine and H1 receptor antagonists
INVENTOR(S): Sanganee, Hitesh; Springthorpe, Brian
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.
SOURCE: PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

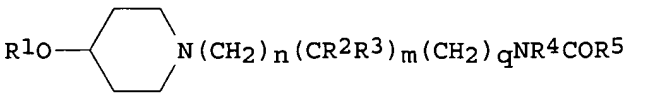
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002020484	A1	20020314	WO 2001-SE1869	20010830

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2000-21670 A 20000904

GI



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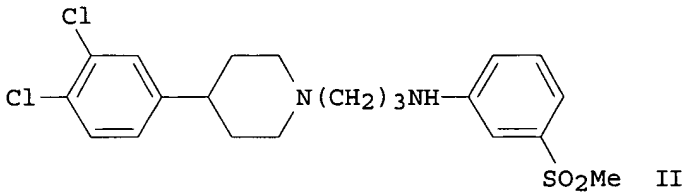


II

AB Title compds. I [R1 = (un)substituted Ph; n = 1-4; m = 0, 1; when m = 0, q = 0; when m = 1, q = 1-4; R2, R3 = H, alkyl, R4 = H, alkyl, cycloalkylalkyl, R5 = substituted cyclic, heterocyclic; R2 = (un)substituted Ph, R3 = H, alkyl, R4 = H, alkyl, alkoxy, R5 = substituted cyclic, heterocyclic] were prepd. for use as chemokine and H1 receptor antagonists in the treatment of asthma and rhinitis (no data). Thus, 3,4-Cl2C6H3OH was treated with 1-tert.-butoxycarbonyl-4-piperidinol, deblocked, treated with Br(CH2)3NHBoc, and deblocked to give the piperidine II as its hydrochloride.

IT **404031-40-9P**

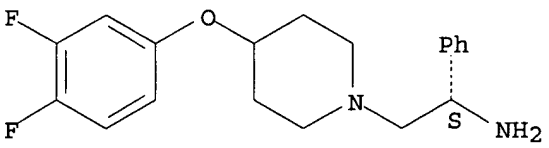
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of acylaminoalkylpiperidines as chemokine and H1 receptor antagonists)

RN 404031-40-9 CA

CN 1-Piperidineethanamine, 4-(3,4-difluorophenoxy)-.alpha.-phenyl-, (.alpha.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **404031-40-9P 404032-32-2P 404032-35-5P 404032-36-6P 404032-37-7P 404032-38-8P 404032-39-9P 404032-40-2P 404032-41-3P 404032-42-4P 404032-43-5P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of acylaminoalkylpiperidines as chemokine and H1 receptor

antagonists)

IT 404030-06-4P 404030-07-5P 404030-08-6P
404030-09-7P 404030-10-0P 404030-11-1P
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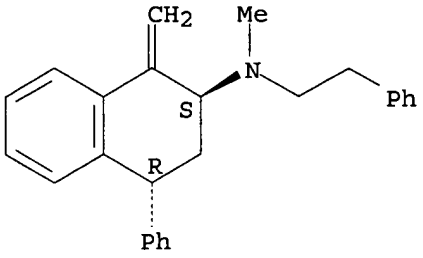
404032-28-6P 404032-29-7P 404032-44-6P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of acylaminoalkylpiperidines as chemokine and H1 receptor antagonists)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 36 CA COPYRIGHT 2002 ACS
ACCESSION NUMBER: 136:243285 CA
TITLE: QSAR study on binding affinity of PATs (rodenticides) to the [3H]-mepyramine-labelled H1 receptor in rat and guinea pig brain
AUTHOR(S): Agrawal, V. K.; Karmarkar, S.; Khadikar, P. V.
CORPORATE SOURCE: Department of Chemistry, A.P.S. University, Rewa, 486 003, India
SOURCE: SAR and QSAR in Environmental Research (2001), 12(6), 529-545
CODEN: SQERED; ISSN: 1062-936X
PUBLISHER: Gordon & Breach Science Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The binding of a series of phenylaminotetralin (PAT) analogs (rodenticides) to the [3H]-mepyramine-labeled H1 receptor in rat and guinea pig brain was investigated topol. using negentropy (N), mol. redundancy (MRI), first-order mol. connectivity (1.chi.v), Wiener (W), and Szeged (Sz) indexes. Multiple regression analyses showed that MRI provided excellent results upon introduction of indicator parameters. Predictive ability of the proposed models was discussed using cross-validation parameters.
IT **404581-06-2**
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(binding affinity to H1 receptor in rat and guinea pig brain; QSAR study on)
RN 404581-06-2 CA
CN 2-Naphthalenamine, 1,2,3,4-tetrahydro-N-methyl-1-methylene-4-phenyl-N-(2-phenylethyl)-, (2R,4S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



IT **404581-06-2 404581-07-3 404581-08-4**
404581-16-4 404581-17-5
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(binding affinity to H1 receptor in rat and guinea pig brain; QSAR study on)
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 36 CA COPYRIGHT 2002 ACS
ACCESSION NUMBER: 136:215424 CA
TITLE: Cyclized peptides of IgE for allergy immunotherapy
INVENTOR(S): Friede, Martin; Mason, Sean; Turnell, William Gordon; Vinals y Bassols, Carlota
PATENT ASSIGNEE(S): Smithkline Beecham Biologicals S.A., Belg.; Peptide Therapeutics Limited
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002016409	A2	20020228	WO 2001-EP9576	20010817

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2000-20717 A 20000822
OTHER SOURCE(S): MARPAT 136:215424
AB The authors disclose a process for the covalent conjugation of disulfide bridge cyclized peptides to immunogenic carrier mols. by thioether linkages to form vaccine immunogens. In particular, the process involves reacting a thiolated carrier with a maleimide-derivatized cyclic peptide. In one example, the authors prep. immunogens based on peptides derived from the sequence of human IgE. Immunization with the cyclic peptide-carrier protein produced IgG antibodies with the ability to block **histamine** release by human basophils.
IT **401910-48-3**
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

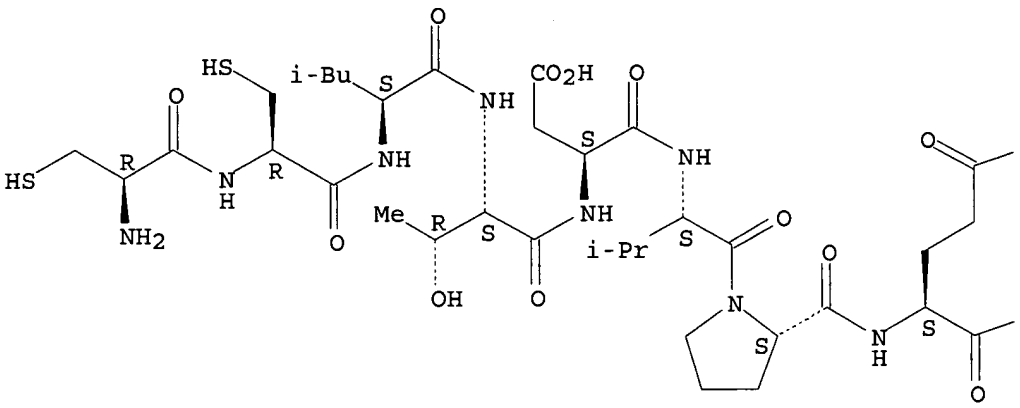
(disulfide bridge cyclization and conjugation to immunol. carriers)

RN 401910-48-3 CA

CN L-Aspartic acid, L-cysteinyl-L-cysteinyl-L-leucyl-L-threonyl-L-.alpha.-aspartyl-L-valyl-L-prolyl-L-glutaminylglycyl-L-valyl-L-methionyl-L-tyrosyl-L-lysylglycyl-L-seryl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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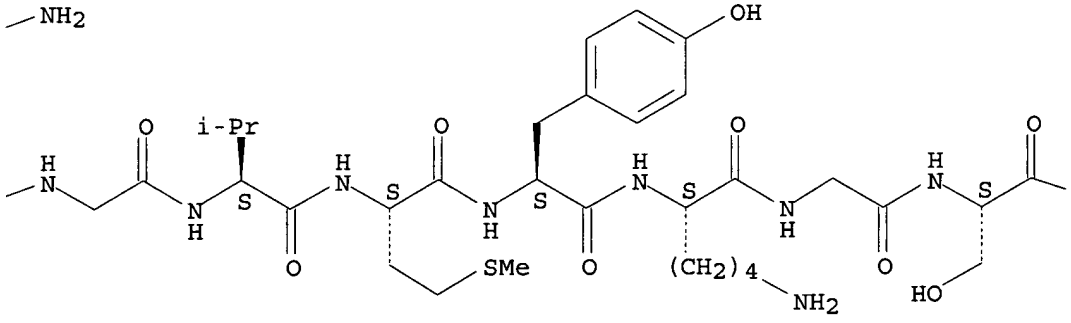

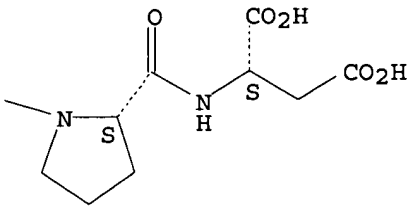

IT **401910-48-3 401910-49-4 401910-50-7**
401910-51-8
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(disulfide bridge cyclization and conjugation to immunol. carriers)

IT **401910-52-9 401910-53-0 401910-54-1**
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401914-12-3
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(immunogens of disulfide bridge cyclized peptides of IgE conjugated by thioether linkage to immunol. carriers)

L4 ANSWER 8 OF 36 CA COPYRIGHT 2002 ACS
ACCESSION NUMBER: 136:213112 CA
TITLE: Gramicidin derivatives as membrane-based pH sensors
AUTHOR(S): Borisenko, Vitali; Zhang, Zhihua; Woolley, G. Andrew
CORPORATE SOURCE: Department of Chemistry, University of Toronto, Toronto, ON, M5S 3H6, Can.
SOURCE: Biochimica et Biophysica Acta (2002), 1558(1), 26-33
CODEN: BBACAQ; ISSN: 0006-3002
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Ion channels provide a means for sensitive pH measurement at membrane interfaces. Detailed knowledge of the structure and function of gramicidin channels permits the engineering of pH-sensitive derivs. Two derivs., gramicidin-ethylenediamine and gramicidin-**histamine**, are shown to exhibit pH-dependent single-channel behavior over the pH ranges 9-11 and 6.5-8.5, resp. Thermal isomerization of a carbamate group at the entrance of the channels leads to a pattern of steps in single-channel recordings. The size of the steps depends on the time-averaged degree of protonation of the appended group (ethylenediamine

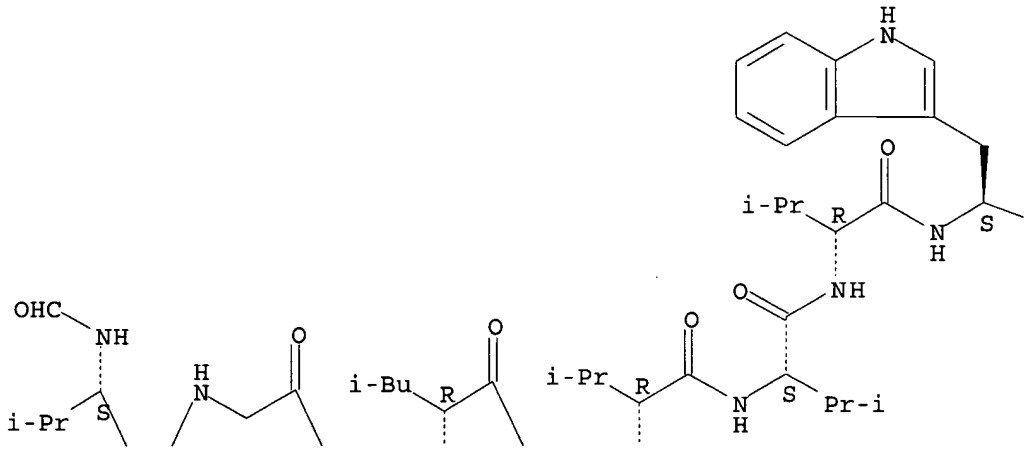
or **histamine**). Measurement of the size of the steps thus permits single-mol. pH sensing under sym. pH conditions or in the presence of a pH gradient.

IT **402789-36-0P**
RL: ARU (Analytical role, unclassified); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation)
(7; gramicidin derivs. as membrane-based pH sensors)

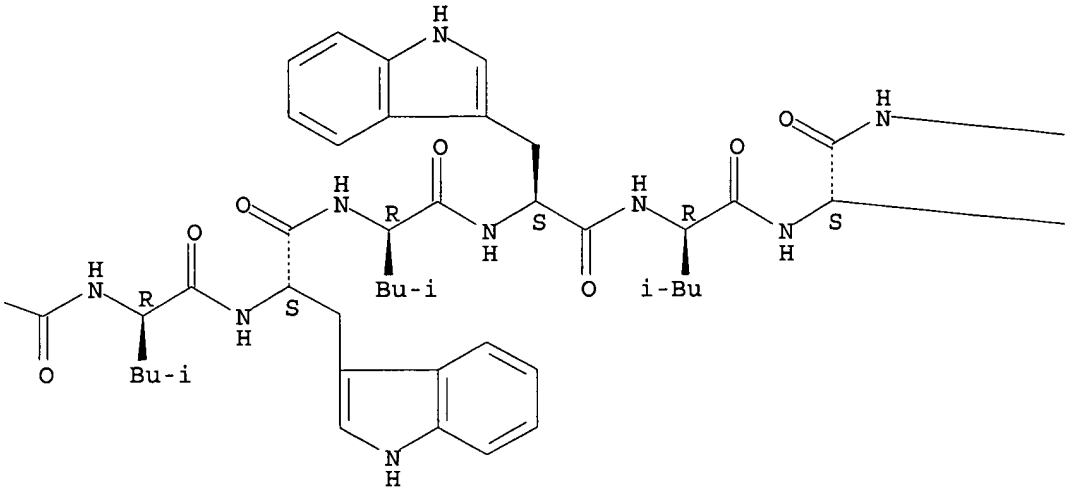
RN 402789-36-0 CA
CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.

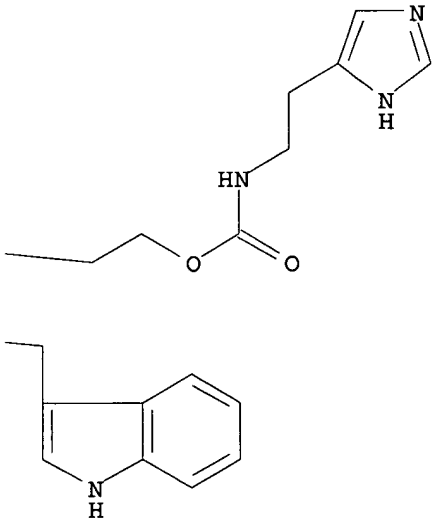
PAGE 1-A

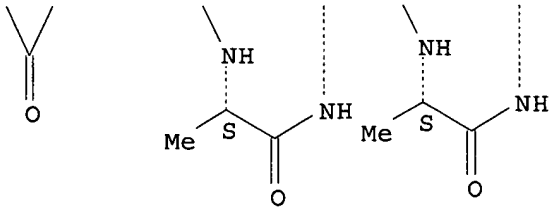


PAGE 1-B



PAGE 1-C



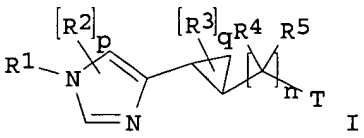


IT **402789-36-0P**
RL: ARU (Analytical role, unclassified); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation)
(7; gramicidin derivs. as membrane-based pH sensors)
REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 36 CA COPYRIGHT 2002 ACS
ACCESSION NUMBER: 136:200185 CA
TITLE: Preparation of novel alicyclic imidazoles as **histamine** H3 agents
INVENTOR(S): Rong, Yajing; Jiang, Jack B.; Ali, Syed M.
PATENT ASSIGNEE(S): Gliatech, Inc., USA
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002013821	A1	20020221	WO 2001-US41738	20010815
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002042400	A1	20020411	US 2001-930644	20010815

PRIORITY APPLN. INFO.: US 2000-225968P P 20000817
OTHER SOURCE(S): MARPAT 136:200185
GI



AB The title compds. [I; n = 0-6; p = 0-2; q = 0-4; T = H, OH, CN, etc.; R1 = H, OH, alkyl, etc.; R2-R5 = H, halo, OH, etc.] useful for the control or

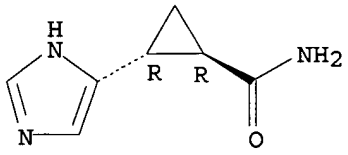
prevention of disease states in which **histamine** H3 receptors are involved, such as allergy, inflammation, hypotension, glaucoma, sleeping disorders, states of hyper- and hypo-motility of the gastro-intestinal tract, cardiovascular disease, hypo- and hyper-activity of the central nervous system, Alzheimer's, schizophrenia, obesity and migraines, were prepd. Thus, treating 2-[1-(triphenylmethyl)imidazol-4-yl]cyclopropanecarbaldehyde with NH2OH.HCl in the presence of Et3N in MeCN followed by addn. of phthalic anhydride (64%), and trityl group removal (55%) afforded trans-I.TFA [n, p, q = 0; T = CN; R1 = H] which showed Ki of 20 nM against **histamine** H3 receptor binding.

IT **400779-33-1P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of novel alicyclic imidazoles as **histamine** H3 agents)

RN 400779-33-1 CA

CN Cyclopropanecarboxamide, 2-(1H-imidazol-4-yl)-, (1R,2R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



IT **400779-33-1P 400779-34-2P 400779-35-3P**
400779-36-4P 400779-42-2P 400779-43-3P
400779-45-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of novel alicyclic imidazoles as **histamine** H3 agents)

IT **400779-48-8P 400779-52-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of novel alicyclic imidazoles as **histamine** H3 agents)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 36 CA COPYRIGHT 2002 ACS
ACCESSION NUMBER: 136:200184 CA
TITLE: Preparation of pyrazolo[1,5-a]pyridines as protein kinase inhibitors for treatment of inflammatory and autoimmune diseases
INVENTOR(S): Alberti, Michael John; Baldwin, Ian Robert; Cheung, Mui; Cockerill, Stuart; Flack, Stephen; Harris, Philip Anthony; Jung, David Kendall; Peckham, Gregory; Peel, Michael Robert; Stanford, Jennifer Badiang; Stevens, Kirk; Veal, James Marvin
PATENT ASSIGNEE(S): Glaxo Group Limited, UK
SOURCE: PCT Int. Appl., 173 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002016359	A1	20020228	WO 2001-GB3783	20010822

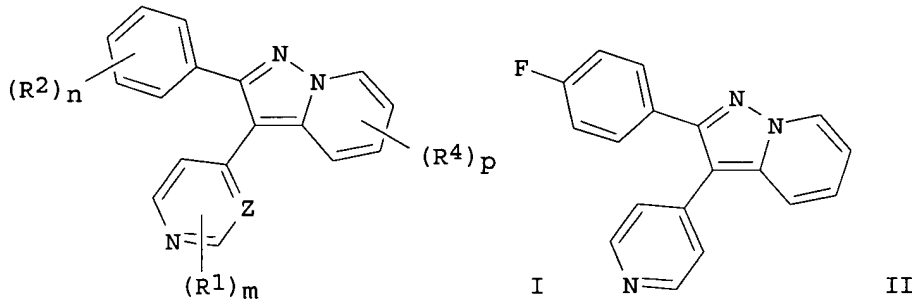
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2000-20556 A 20000822
GB 2000-20576 A 20000822

OTHER SOURCE(S): MARPAT 136:200184

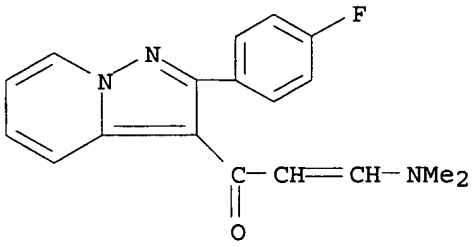
GI



AB Title compds. I [wherein Z = CH or N; m = 1-2; n = 1-3; p = 1-3; R1 = independently Xd(CH2)eR5; d = 0-1; e = 0-6; X = O, NR6, or SO0-2; R3 = H, halo, OH, CN, NO2, trihalomethyl, or (un)substituted (cyclo)alkyl, alkenyl, alkynyl, heterocyclyl, (hetero)aryl, phthalimido, aminophenyl, aminobenzyl, acyl(oxy), carbamoyl(oxy), carboxylate, sulfamoyl, carboximidamido, etc.; R4 = independently Yd(CH2)eR3; R5 = H, halo, OH, CN, NO2, trihalomethyl, or (un)substituted (cyclo)alkyl, alkenyl, alkynyl, heterocyclyl, (hetero)aryl, amino, aminophenyl, aminobenzyl, acyl(oxy), carbamoyl(oxy), carboximidamido, acylamino, sulfamoyl, etc.; R6 = H, (cyclo)alkyl, alkenyl, (hetero)aryl, or heterocyclyl; or their salts, solvates, or physiol. functional derivs. thereof] were prepd. as p38 and JNK3 protein kinase inhibitors. For example, cycloaddn. of Me 3-(4-fluorophenyl)propiolate (2-step prepn. given) and 1-aminopyridinium iodide in AcCN in the presence of 1,8-diazabicycloundec-7-ene gave Me 2-(4-fluorophenyl)pyrazolo[1,5-a]pyridine-3-carboxylate (70%), which was hydrolyzed to the acid (100%). Reaction with sodium bicarbonate, followed by N-bromosuccinimide, in DMF afforded the bromo deriv. (80%). Reductive addn. of 4-(tributylstannyl)pyridine using Pd(PPh3)4 in toluene gave II (80%). The latter inhibited p38 kinase and tumor necrosis factor (TNF) release from human peripheral blood mononuclear cells following stimulation with lipopolysaccharide with IC50 values of < 0.5 .mu.M. I are useful for the treatment of inflammatory and autoimmune diseases, cancer, and a variety of other conditions related to regulation of p38 kinase and/or JNK kinase.

IT **401816-43-1P**, 2-(4-Fluorophenyl)-3-[3-(dimethylamino)-2-

propenoyl]pyrazolo[1,5-a]pyridine
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of pyrazolo[1,5-a]pyridines as protein kinase inhibitors for treatment of inflammatory and autoimmune diseases)
RN 401816-43-1 CA
CN 2-Propen-1-one, 3-(dimethylamino)-1-[2-(4-fluorophenyl)pyrazolo[1,5-a]pyridin-3-yl]- (9CI) (CA INDEX NAME)



IT **401816-43-1P**, 2-(4-Fluorophenyl)-3-[3-(dimethylamino)-2-propenoyl]pyrazolo[1,5-a]pyridine **401816-47-5P**, 2-(4-Fluorophenyl)-3-[3-(dimethylamino)-2-propenoyl]-6-trifluoromethylpyrazolo[1,5-a]pyridine **401816-55-5P**, 4-[2-(4-Fluorophenyl)-6-trifluoromethylpyrazolo[1,5-a]pyridin-3-yl]-N-[3-(4-methoxybenzyloxy)propyl]-2-pyrimidinamine **401816-59-9P**, 2-(4-Fluorophenyl)-3-[3-(dimethylamino)-2-propenoyl]-6-cyanopyrazolo[1,5-a]pyridine **401816-63-5P** **401816-64-6P** **401816-70-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of pyrazolo[1,5-a]pyridines as protein kinase inhibitors for treatment of inflammatory and autoimmune diseases)
IT **401816-68-0P**, N-[3-(4-Methylpiperazino)propyl]-4-[2-(4-fluorophenyl)-6-trifluoromethylpyrazolo[1,5-a]pyridin-3-yl]-2-pyrimidinamine
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(protein kinase inhibitor; prepn. of pyrazolo[1,5-a]pyridines as protein kinase inhibitors for treatment of inflammatory and autoimmune diseases)
IT **401815-99-4P**, 4-[2-(4-Fluorophenyl)pyrazolo[1,5-a]pyridin-3-yl]-N-[2-(1H-imidazol-5-yl)ethyl]-2-pyridinamine **401816-00-0P**, N-Butyl-4-[2-(4-fluorophenyl)pyrazolo[1,5-a]pyridin-3-yl]-2-pyridinamine **401816-01-1P**, 3-[4-[2-(4-Fluorophenyl)pyrazolo[1,5-a]pyridin-3-yl]-2-pyridinylamino]-1-propanol **401816-03-3P**, N1-4-[2-(4-Fluorophenyl)pyrazolo[1,5-a]pyridin-3-yl]-2-pyridinyl-1,3-propanediamine **401816-05-5P**, 4-[2-(4-Fluorophenyl)pyrazolo[1,5-a]pyridin-3-yl]-N-hexyl-2-pyridinamine **401816-07-7P**, 4-[2-(4-Fluorophenyl)pyrazolo[1,5-a]pyridin-3-yl]-N-pentyl-2-pyridinamine **401816-09-9P**, 4-[2-(4-Fluorophenyl)pyrazolo[1,5-a]pyridin-3-yl]-N-propyl-2-pyridinamine **401816-11-3P**, N1-4-[2-(4-Fluorophenyl)pyrazolo[1,5-a]pyridin-3-yl]-2-pyridinyl-1,4-butanediamine **401816-12-4P**, 2-[4-[2-(4-Fluorophenyl)pyrazolo[1,5-a]pyridin-3-yl]-2-pyridinylamino]-1-ethanol **401816-19-1P**, 4-[2-(4-Fluorophenyl)-6-trifluoromethylpyrazolo[1,5-a]pyridin-3-yl]-N-isopropyl-2-pyridinamine **401816-22-6P**, 3-[4-[2-(4-Fluorophenyl)-6-trifluoromethylpyrazolo[1,5-a]pyridin-3-yl]-2-pyridinylamino]-1-propanol **401816-25-9P**, N-(3-Aminopropyl)-4-[6-bromo-2-(4-

fluorophenyl)pyrazolo[1,5-a]pyridin-3-yl]-2-pyridinamine **401816-28-2P**, 2-(4-Fluorophenyl)-3-(4-pyridinyl)pyrazolo[1,5-a]pyridine-6-carboxamide **401816-37-3P**, N-Butyl-4-[2-(4-fluorophenyl)pyrazolo[1,5-a]pyridin-3-yl]-2-pyrimidinamine **401816-40-8P**, 4-[2-(4-Fluorophenyl)pyrazolo[1,5-a]pyridin-3-yl]-N-(2-propyl)-2-pyrimidinamine **401816-48-6P**, N-Butyl-4-[2-(4-fluorophenyl)-6-trifluoromethylpyrazolo[1,5-a]pyridin-3-yl]-2-pyrimidinamine **401816-51-1P**, 4-[2-(4-Fluorophenyl)-6-trifluoromethylpyrazolo[1,5-a]pyridin-3-yl]-N-(2-propyl)-2-pyrimidinamine **401816-52-2P**, 4-[2-(4-Fluorophenyl)-6-trifluoromethylpyrazolo[1,5-a]pyridin-3-yl]-N-(2-propenyl)-2-pyrimidinamine **401816-53-3P**, 4-[2-(4-Fluorophenyl)-6-trifluoromethylpyrazolo[1,5-a]pyridin-3-yl]-N-(2,2,2-trifluoroethyl)-2-pyrimidinamine **401816-54-4P**, 3-[4-[2-(4-Fluorophenyl)-6-trifluoromethylpyrazolo[1,5-a]pyridin-3-yl]-2-pyrimidinylamino]-1-propanol **401816-61-3P**, 2-(4-Fluorophenyl)-3-[2-(cyclopropylamino)-4-pyrimidinyl]-6-pyrazolo[1,5-a]pyridinylcarboxamide **401816-62-4P**, 2-(4-Fluorophenyl)-3-[2-[(3-hydroxypropyl)amino]-4-pyrimidinyl]-6-pyrazolo[1,5-a]pyridinylcarboxamide **401816-67-9P**, 2-(4-Fluorophenyl)-3-[2-[[3-(4-methylpiperazino)propyl]amino]-4-pyrimidinyl]-6-pyrazolo[1,5-a]pyridinylcarboxamide **401816-71-5P**, 4-[2-(4-Fluorophenyl)pyrazolo[1,5-a]pyridin-3-yl]-N-[2-(1H-imidazol-5-yl)ethyl]-2-pyrimidinamine **401816-79-3P**, N-[3-(Dimethylamino)propyl]-N-[4-[2-(4-fluorophenyl)-6-(trifluoromethyl)pyrazolo[1,5-a]pyridin-3-yl]pyrimidin-2-yl]amine **401816-80-6P**, N-[3-(Dimethylamino)propyl]-N-[4-[6-(trifluoromethyl)-2-[4-(trifluoromethyl)phenyl]pyrazolo[1,5-a]pyridin-3-yl]pyrimidin-2-yl]amine **401816-85-1P**, N-[4-[2-(3-Chloro-4-fluorophenyl)-6-(trifluoromethyl)pyrazolo[1,5-a]pyridin-3-yl]pyrimidin-2-yl]-N-[3-(dimethylamino)propyl]amine **401816-89-5P**, N-[4-[2-(3-Chlorophenyl)-6-(trifluoromethyl)pyrazolo[1,5-a]pyridin-3-yl]pyrimidin-2-yl]-N-[3-(dimethylamino)propyl]amine **401816-93-1P**, N-[4-[2-(4-Fluorophenyl)-6-(trifluoromethyl)pyrazolo[1,5-a]pyridin-3-yl]pyrimidin-2-yl]-N-[2-(dimethylamino)ethyl]amine **401816-95-3P**, N-[4-(Diethylamino)butyl]-N-[4-[6-(trifluoromethyl)-2-[4-(trifluoromethyl)phenyl]pyrazolo[1,5-a]pyridin-3-yl]pyrimidin-2-yl]amine **401816-96-4P**, N-[4-[2-(3-Chloro-4-fluorophenyl)-6-(trifluoromethyl)pyrazolo[1,5-a]pyridin-3-yl]pyrimidin-2-yl]-N-[4-(diethylamino)butyl]amine **401816-97-5P**, N-[4-[2-(3-Chlorophenyl)-6-(trifluoromethyl)pyrazolo[1,5-a]pyridin-3-yl]pyrimidin-2-yl]-N-[4-(diethylamino)butyl]amine **401816-98-6P**, N-[2-(Diethylamino)ethyl]-N-[4-[6-(trifluoromethyl)-2-[4-(trifluoromethyl)phenyl]pyrazolo[1,5-a]pyridin-3-yl]pyrimidin-2-yl]amine **401816-99-7P**, N-[4-[2-(3-Chlorophenyl)-6-(trifluoromethyl)pyrazolo[1,5-a]pyridin-3-yl]pyrimidin-2-yl]-N-[2-(diethylamino)ethyl]amine **401817-00-3P**, N-[2-(Dipropylamino)ethyl]-N-[4-[6-(trifluoromethyl)-2-[4-(trifluoromethyl)phenyl]pyrazolo[1,5-a]pyridin-3-yl]pyrimidin-2-yl]amine **401817-01-4P**, N-[4-[2-(3-Chloro-4-fluorophenyl)-6-(trifluoromethyl)pyrazolo[1,5-a]pyridin-3-yl]pyrimidin-2-yl]-N-[2-(dipropylamino)ethyl]amine **401817-02-5P**, N-[4-[2-(3-Chlorophenyl)-6-(trifluoromethyl)pyrazolo[1,5-a]pyridin-3-yl]pyrimidin-2-yl]-N-[2-(dipropylamino)ethyl]amine **401817-03-6P**, N-[4-[2-(3-Chloro-4-fluorophenyl)-6-(trifluoromethyl)pyrazolo[1,5-a]pyridin-3-yl]pyrimidin-2-yl]-N-[2-(diisopropylamino)ethyl]amine **401817-04-7P**, N-[4-[2-(3-Chlorophenyl)-6-(trifluoromethyl)pyrazolo[1,5-a]pyridin-3-yl]pyrimidin-2-yl]-N-[2-(diisopropylamino)ethyl]amine **401817-05-8P**, N-[4-[2-(4-Fluorophenyl)-6-(trifluoromethyl)pyrazolo[1,5-a]pyridin-3-yl]pyrimidin-2-yl]-N-(2-pyrrolidin-1-ylethyl)amine **401817-06-9P**, N-(2-Pyrrolidin-1-ylethyl)-N-[4-[6-(trifluoromethyl)-2-[4-

(trifluoromethyl)phenyl]pyrazolo[1,5-a]pyridin-3-yl]pyrimidin-2-yl]amine **401817-07-0P 401817-08-1P**, N-[4-[2-(3-Chlorophenyl)-6-(trifluoromethyl)pyrazolo[1,5-a]pyridin-3-yl]pyrimidin-2-yl]-N-(2-pyrrolidin-1-ylethyl)amine **401817-09-2P**, N-[4-[2-(3-Chlorophenyl)-6-(trifluoromethyl)pyrazolo[1,5-a]pyridin-3-yl]pyrimidin-2-yl]-N-(4-pyrrolidin-1-ylbutyl)amine **401817-10-5P**, N-[4-[2-(4-Fluorophenyl)-6-(trifluoromethyl)pyrazolo[1,5-a]pyridin-3-yl]pyrimidin-2-yl]-N-(2-piperidin-1-ylethyl)amine **401817-11-6P**, N-(2-Piperidin-1-ylethyl)-N-[4-[6-(trifluoromethyl)-2-[4-(trifluoromethyl)phenyl]pyrazolo[1,5-a]pyridin-3-yl]pyrimidin-2-yl]amine **401817-12-7P**, N-[4-[2-(3-Chloro-4-fluorophenyl)-6-(trifluoromethyl)pyrazolo[1,5-a]pyridin-3-yl]pyrimidin-2-yl]-N-(2-piperidin-1-ylethyl)amine **401817-13-8P**, N-[4-[2-(3-Chlorophenyl)-6-(trifluoromethyl)pyrazolo[1,5-a]pyridin-3-yl]pyrimidin-2-yl]-N-(2-piperidin-1-ylethyl)amine **401817-14-9P**, N-[4-[2-(4-Fluorophenyl)-6-(trifluoromethyl)pyrazolo[1,5-a]pyridin-3-yl]pyrimidin-2-yl]-N-(3-piperidin-1-ylpropyl)amine **401817-15-0P**, N-(3-Piperidin-1-ylpropyl)-N-[4-[6-(trifluoromethyl)-2-[4-(trifluoromethyl)phenyl]pyrazolo[1,5-a]pyridin-3-yl]pyrimidin-2-yl]amine **401817-16-1P**, N-[4-[2-(3-Chloro-4-fluorophenyl)-6-(trifluoromethyl)pyrazolo[1,5-a]pyridin-3-yl]pyrimidin-2-yl]-N-(3-piperidin-1-ylpropyl)amine **401817-18-3P**, N-[4-[2-(3-Chlorophenyl)-6-(trifluoromethyl)pyrazolo[1,5-a]pyridin-3-yl]pyrimidin-2-yl]-N-(3-piperidin-1-ylpropyl)amine **401817-19-4P**, N-(2-Azepan-1-ylethyl)-N-[4-[6-(trifluoromethyl)-2-[4-(trifluoromethyl)phenyl]pyrazolo[1,5-a]pyridin-3-yl]pyrimidin-2-yl]amine **401817-20-7P**, N-(2-Azepan-1-ylethyl)-N-[4-[2-(3-chloro-4-fluorophenyl)-6-(trifluoromethyl)pyrazolo[1,5-a]pyridin-3-yl]pyrimidin-2-yl]amine **401817-21-8P**, N-(2-Azepan-1-ylethyl)-N-[4-[2-(3-chlorophenyl)-6-(trifluoromethyl)pyrazolo[1,5-a]pyridin-3-yl]pyrimidin-2-yl]amine **401817-22-9P**, N-[4-[2-(4-Fluorophenyl)-6-(trifluoromethyl)pyrazolo[1,5-a]pyridin-3-yl]pyrimidin-2-yl]-N-(2-morpholin-4-ylethyl)amine **401817-23-0P**, N-(2-Morpholin-4-ylethyl)-N-[4-[6-(trifluoromethyl)-2-[4-(trifluoromethyl)phenyl]pyrazolo[1,5-a]pyridin-3-yl]pyrimidin-2-yl]amine **401817-24-1P**, N-[4-[2-(3-Chloro-4-fluorophenyl)-6-(trifluoromethyl)pyrazolo[1,5-a]pyridin-3-yl]pyrimidin-2-yl]-N-(2-morpholin-4-ylethyl)amine **401817-25-2P**, N-(3-Morpholin-4-ylpropyl)-N-[4-[6-(trifluoromethyl)-2-[4-(trifluoromethyl)phenyl]pyrazolo[1,5-a]pyridin-3-yl]pyrimidin-2-yl]amine **401817-26-3P**, N-[4-[2-(3-Chloro-4-fluorophenyl)-6-(trifluoromethyl)pyrazolo[1,5-a]pyridin-3-yl]pyrimidin-2-yl]-N-(3-morpholin-4-ylpropyl)amine **401817-27-4P**, N-[4-[2-(3-Chlorophenyl)-6-(trifluoromethyl)pyrazolo[1,5-a]pyridin-3-yl]pyrimidin-2-yl]-N-(3-morpholin-4-ylpropyl)amine **401817-28-5P**, N-[4-[2-(3-Chloro-4-fluorophenyl)-6-(trifluoromethyl)pyrazolo[1,5-a]pyridin-3-yl]pyrimidin-2-yl]-N-[3-(4-methylpiperazin-1-yl)propyl]amine **401817-29-6P**, N-[4-[2-(4-Fluorophenyl)-6-(trifluoromethyl)pyrazolo[1,5-a]pyridin-3-yl]pyrimidin-2-yl]-N-[2-(4-methylpiperazin-1-yl)ethyl]amine **401817-31-0P**, N-[2-(4-Propylpiperazin-1-yl)ethyl]-N-[4-[6-(trifluoromethyl)-2-[4-(trifluoromethyl)phenyl]pyrazolo[1,5-a]pyridin-3-yl]pyrimidin-2-yl]amine **401817-32-1P**, N-[4-[2-(3-Chloro-4-fluorophenyl)-6-(trifluoromethyl)pyrazolo[1,5-a]pyridin-3-yl]pyrimidin-2-yl]-N-[2-(4-propylpiperazin-1-yl)ethyl]amine **401817-33-2P**, N-[4-[2-(3-Chlorophenyl)-6-(trifluoromethyl)pyrazolo[1,5-a]pyridin-3-yl]pyrimidin-2-yl]-N-[2-(4-propylpiperazin-1-yl)ethyl]amine
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(protein kinase inhibitor; prepn. of pyrazolo[1,5-a]pyridines as

protein kinase inhibitors for treatment of inflammatory and autoimmune diseases)

IT **401816-56-6**, N-[3-(4-Methoxybenzyloxy)propyl]guanidine
401816-69-1, N-[3-(4-Methylpiperazino)propyl]guanidine hydrogen sulfate **401817-30-9**, [2-(4-Methylpiperazin-1-yl)ethyl]amine hydrochloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; prepn. of pyrazolo[1,5-a]pyridines as protein kinase inhibitors for treatment of inflammatory and autoimmune diseases)

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

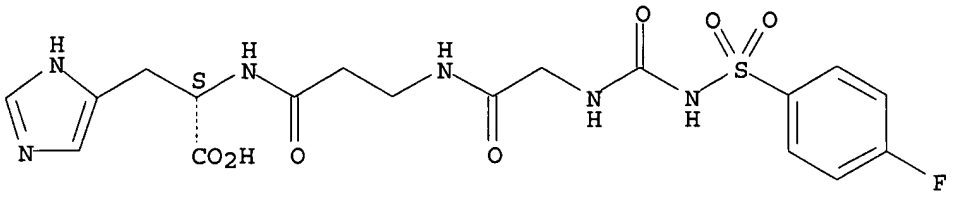
L4 ANSWER 11 OF 36 CA COPYRIGHT 2002 ACS
ACCESSION NUMBER: 136:196078 CA
TITLE: Carbonic Anhydrase Activators: High Affinity Isozymes I, II, and IV Activators, Incorporating a .beta.-Alanyl-histidine Scaffold
AUTHOR(S): Scozzafava, Andrea; Supuran, Claudiu T.
CORPORATE SOURCE: Laboratorio di Chimica Inorganica e Bioinorganica, Universita degli Studi, Florence, I-50121, Italy
SOURCE: Journal of Medicinal Chemistry (2002), 45(2), 284-291
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A novel class of tight binding carbonic anhydrase (CA) activators was designed by using **histamine** and histidine as lead mols. Carnosine (.beta.-Ala-His) derivs. were synthesized by reaction of appropriately derivatized .beta.-alanines with imidazole/carboxy-protected histidine in the presence of carbodiimides, followed by removal of the various protecting groups. The derivatized .beta.-alanines mentioned above were in turn obtained by coupling of 4-fluorophenylsulfonylureido amino acids (fpu-AA) or 2-toluenesulfonylureido amino acids (ots-AA) with .beta.-Ala. Some structurally related dipeptides with the general formula fpu/ots-AA1-AA2 (AA, AA1, and AA2 represent amino acyl moieties) were also prepd. by a similar strategy and used thereafter for obtaining CA activators incorporating a modified tetrapeptide scaffold. Many of the new tri-/tetrapeptide derivs. reported here proved to be efficient in vitro activators of three CA isoenzymes. Very good activity was detected against hCA I and bCA IV, for which some of the new compds. showed affinities in the 1-20 nM range (h = human; b = bovine isoenzymes), whereas against hCA II, their affinities were in the range of 10-40 nM. Ex vivo expts. showed some of the new activators to strongly enhance cytosolic red cell CA activity after incubation with human erythrocytes. This new class of CA activators might lead to the development of drugs/diagnostic tools for the management of CA deficiency syndromes, as well as for the pharmacol. enhancement of synaptic efficacy, spatial learning, and memory. This may constitute a new approach for the treatment of Alzheimer's disease and other conditions in need of achieving memory therapy.

IT **400859-14-5P**
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(activation of carbonic anhydrase isoenzymes I II and IV by .beta.-alanyl-histidine scaffold derivs.)

RN 400859-14-5 CA
CN L-Histidine, N-[[[(4-fluorophenyl)sulfonyl]amino]carbonyl]glycyl-.beta.-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **400859-14-5P 400859-15-6P 400859-17-8P**
400859-18-9P 400859-19-0P 400859-20-3P
400859-21-4P 400859-22-5P 400859-23-6P
400859-24-7P 400859-25-8P 400859-26-9P
400859-27-0P 400859-28-1P 400859-29-2P
400859-31-6P 400859-32-7P 400859-33-8P
400859-34-9P 400859-35-0P 400859-36-1P
400859-37-2P 400859-38-3P 400859-39-4P
400859-40-7P 400859-41-8P 400859-42-9P
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400859-49-6P 400859-50-9P 400859-51-0P
400859-52-1P 400859-53-2P 400859-54-3P
400859-55-4P 400859-56-5P 400859-57-6P
400859-58-7P 400859-59-8P 400859-60-1P
400859-61-2P 400859-62-3P 400859-63-4P
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation);
BIOL (Biological study); PREP (Preparation)
(activation of carbonic anhydrase isoenzymes I II and IV by
.beta.-alanyl-histidine scaffold derivs.)

IT **400859-13-4 400859-65-6 400859-66-7**
400859-67-8 400859-68-9 400859-69-0
400859-70-3 400859-71-4 400859-72-5
400859-73-6 400859-74-7 400859-76-9
400859-77-0 400859-78-1 400859-79-2
400859-80-5 400859-81-6 400859-82-7
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400859-89-4 400859-90-7 400859-91-8
400859-93-0 400859-95-2 400859-97-4
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400860-11-9 400860-13-1 400860-14-2
400860-16-4 400860-18-6 400860-24-4
400860-26-6 400860-28-8 400860-30-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(activation of carbonic anhydrase isoenzymes I II and IV by
.beta.-alanyl-histidine scaffold derivs.)

IT **400859-10-1P 400859-11-2P 400859-12-3P**
400860-32-4P 400860-35-7P 400860-37-9P
400860-39-1P 400860-41-5P 400860-43-7P
400860-45-9P 400860-47-1P 400860-49-3P
400860-51-7P 400860-57-3P 400860-59-5P
400860-61-9P 400860-63-1P 400860-65-3P
400860-67-5P 400860-69-7P 400860-71-1P
400860-73-3P 400860-75-5P 400860-80-2P
400860-82-4P 400860-84-6P 400860-86-8P
400860-88-0P 400860-90-4P 400860-92-6P
400860-94-8P 400860-97-1P 400860-99-3P
400861-01-0P 400861-03-2P 400861-05-4P

400861-07-6P 400861-09-8P 400861-11-2P
400861-13-4P 400861-15-6P 400861-17-8P
400861-19-0P 400861-21-4P 400861-23-6P
400861-25-8P 400861-27-0P 400861-29-2P
400861-31-6P 400861-33-8P 400861-35-0P
400861-37-2P 400861-40-7P 400861-42-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(activation of carbonic anhydrase isoenzymes I II and IV by .beta.-alanyl-histidine scaffold derivs.)

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

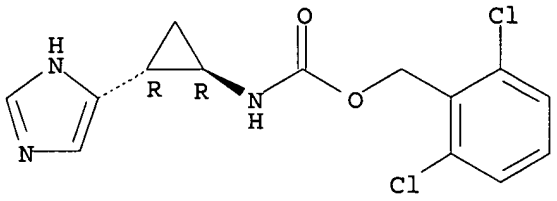
L4 ANSWER 12 OF 36 CA COPYRIGHT 2002 ACS
ACCESSION NUMBER: 136:194263 CA
TITLE: The use of **histamine** H3 receptor inverse agonists for the control of appetite and treatment of obesity
INVENTOR(S): Yates, Stephen L.; Tedford, Clark E.; Brunden, Kurt R.
PATENT ASSIGNEE(S): Gliatech, Inc., USA
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002015905	A1	20020228	WO 2001-US41737	20010815

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-226628P P 20000821
AB A method for the use of **histamine** H3 receptor inverse agonists in the regulation of appetite and treatment of obesity is disclosed. Preferred inverse agonists are imidazole derivs.
IT **401586-44-5**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**histamine** H3 receptor inverse agonists for control of appetite and treatment of obesity)
RN 401586-44-5 CA
CN Carbamic acid, [(1R,2R)-2-(1H-imidazol-4-yl)cyclopropyl]-, (2,6-dichlorophenyl)methyl ester, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



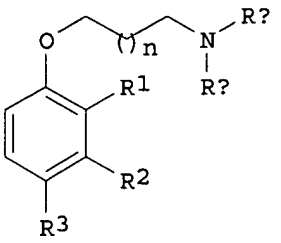
IT **401586-44-5 401586-46-7**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**histamine** H3 receptor inverse agonists for control of appetite and treatment of obesity)
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 13 OF 36 CA COPYRIGHT 2002 ACS
ACCESSION NUMBER: 136:183708 CA
TITLE: Preparation of non-imidazole aryloxyalkylamines as **histamine** H3 receptor antagonists
INVENTOR(S): Apodaca, Richard; Carruthers, Nicholas I.; Dvorak, Curt A.; Rudolph, Dale A.; Shah, Chandravadan R.; Xiao, Wei
PATENT ASSIGNEE(S): Ortho McNeil Pharmaceutical Inc., USA
SOURCE: PCT Int. Appl., 155 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

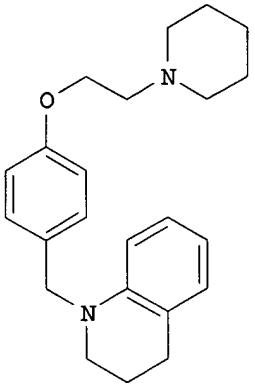
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002012214	A2	20020214	WO 2001-US24655	20010806

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-223768P P 20000808
US 2001-922631 A 20010806
OTHER SOURCE(S): MARPAT 136:183708
GI



I



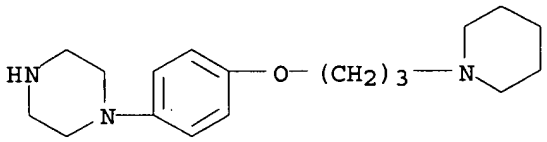
II

AB Title compds. I [Ra-b = alk(en/yn)yl, cycloalkyl; n = 0-4; one of R1-3 = G and the remaining two are H or halo; G = N-contg. heterocycle, e.g., piperidinyl, etc.] were prepd. For instance, 4-(2-(piperidin-1-yl)ethoxy)benzaldehyde was used to alkylate 1,2,3,4-tetrahydroisoquinoline (ClCH2CH2Cl, HOAc, NaBH(OAc)3, 15 h) to give II. II had Ki = 37 nM for the **histamine** H3 receptor. I are useful for treating **histamine**-mediated conditions.

IT **398473-81-9P**, 1-[4-(3-(Piperidin-1-yl)propoxy)phenyl]piperazine hydrochloride
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug; prepn. of non-imidazole aryloxyalkylamines as **histamine** -H3 receptor antagonists)

RN 398473-81-9 CA

CN Piperazine, 1-[4-[3-(1-piperidinyl)propoxy]phenyl]-, monohydrochloride (9CI) (CA INDEX NAME)



HCl

IT **398473-81-9P**, 1-[4-(3-(Piperidin-1-yl)propoxy)phenyl]piperazine hydrochloride **398473-83-1P 398473-99-9P**,

1-[3-(4-Benzyloxyphenoxy)propyl]piperidine **398474-00-5P**, 4-[4-(3-(Pyrrolidin-1-yl)propoxy)phenyl]piperazine-1-carboxylic acid tert-butyl ester **398474-01-6P**, 4-[4-(3-(Piperidin-1-yl)propoxy)phenyl]piperazine-1-carboxylic acid tert-butyl ester **398474-04-9P**, 1-[3-[4-(1H-Pyrrol-2-yl)phenoxy]propyl]piperidine RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug; prepn. of non-imidazole aryloxyalkylamines as **histamine** -H3 receptor antagonists)

IT **398473-15-9P**, Methyl[4-(3-(piperidin-1-yl)propoxy)benzyl](2-pyridin-2-ylethyl)amine **398473-16-0P**, Benzyl methyl[4-(3-(piperidin-1-yl)propoxy)benzyl]amine **398473-17-1P**, Methyl(1-methylpiperidin-4-yl)[4-(3-(piperidin-1-yl)propoxy)benzyl]amine **398473-18-2P**, Ethyl [4-(3-(piperidin-1-yl)propoxy)benzyl] [pyridin-4-yl]methyl amine **398473-19-3P**, [2-(3,4-Dimethoxyphenyl)ethyl] methyl [4-(3-(piperidin-1-yl)propoxy)benzyl]amine **398473-20-6P**, Methyl phenethyl [4-(3-(piperidin-1-yl)propoxy)benzyl]amine **398473-21-7P**, Dimethyl[4-(3-(piperidin-1-yl)propoxy)benzyl]amine **398473-22-8P**, Dimethyl[2-[4-(3-(piperidin-1-yl)propoxy)phenoxy]ethyl]amine **398473-23-9P**, Methyl phenethyl [3-(3-(piperidin-1-yl)propoxy)benzyl]amine **398473-24-0P**, Dibenzyl [3-[2-[4-(3-(piperidin-1-yl)propoxy)phenyl]pyrrol-1-yl]propyl]amine **398473-25-1P**, (Indan-1-yl)[4-(3-(piperidin-1-yl)propoxy)benzyl]amine **398473-26-2P**, Cyclohexyl[4-(3-(piperidin-1-yl)propoxy)benzyl]amine **398473-27-3P**, Cyclopropyl[4-(3-(piperidin-1-yl)propoxy)benzyl]amine **398473-28-4P**, Pyridin-2-yl [4-(3-(pyrrolidin-1-yl)propoxy)benzyl]amine **398473-29-5P**, [4-(3-(Piperidin-1-yl)propoxy)benzyl] [pyridin-2-yl]amine **398473-30-8P**, Phenyl[4-(3-(piperidin-1-yl)propoxy)benzyl]amine **398473-31-9P**, [3-(3-(Piperidin-1-yl)propoxy)benzyl] [pyridin-2-yl]amine **398473-32-0P**, (4-Chlorophenyl)[4-(3-(piperidin-1-yl)propoxy)benzyl]amine **398473-33-1P**, 4-[3-(3-((Piperidin-1-yl)methyl)phenoxy)propyl]morpholine **398473-34-2P**, 1-[3-(4-((Piperidin-1-yl)methyl)phenoxy)propyl]piperidine **398473-35-3P**, Benzyl methyl[1-[4-(3-(piperidin-1-yl)propoxy)benzyl]piperidin-4-yl]amine **398473-36-4P** **398473-37-5P**, 1-[3-[4-[5-((3-(Piperidin-1-yl)propyl)sulfanyl)tetrazol-1-yl]phenoxy]propyl]piperidine **398473-38-6P**, 1-[4-(3-(Piperidin-1-yl)propoxy)benzyl]piperidin-4-ol **398473-39-7P**, 4-[4-(3-(Piperidin-1-yl)propoxy)benzyl]morpholine **398473-40-0P**, 2-[4-(3-(Piperidin-1-yl)propoxy)benzyl]-1,2,3,4-tetrahydroisoquinoline **398473-41-1P**, (1-(4-(3-(Piperidin-1-yl)propoxy)benzyl)piperidin-4-yl)(pyridin-2-yl)amine **398473-42-2P**, 1-Benzyl-4-[4-(3-(piperidin-1-yl)propoxy)benzyl]piperazine **398473-43-3P**, 8-[4-(3-(Piperidin-1-yl)propoxy)benzyl]-1,4-dioxa-8-azaspiro[4.5]decane **398473-44-4P**, 1-[4-(3-(Piperidin-1-yl)propoxy)benzyl]piperidine-4-carboxylic acid amide **398473-45-5P**, 4-Phenyl-1-[4-(3-(piperidin-1-yl)propoxy)benzyl]piperidin-4-ol **398473-46-6P**, 1-Phenyl-4-[4-(3-(piperidin-1-yl)propoxy)benzyl]piperazine **398473-47-7P**, Methyl phenethyl[1-[4-(3-(piperidin-1-yl)propoxy)benzyl]piperidin-4-yl]amine **398473-48-8P**, 2-Methyl-1-(3-(4-((piperidin-1-yl)methyl)phenoxy)propyl)piperidine **398473-49-9P**, [1-[4-(3-(Piperidin-1-yl)propoxy)benzyl]piperidin-4-yl] pyridin-2-yl (2-(pyrrolidin-1-yl)ethyl)amine **398473-50-2P**, 2-[1-[4-(3-(Piperidin-1-yl)propoxy)benzyl]piperidin-4-yl]ethanol **398473-51-3P**, 1-[3-(4-(Pyrrolidin-1-yl)methylphenoxy)propyl]piperidine **398473-52-4P**, 1-[3-[4-(4-Benzylidenepiperidin-1-ylmethyl)phenoxy]propyl]piperidine **398473-53-5P**,

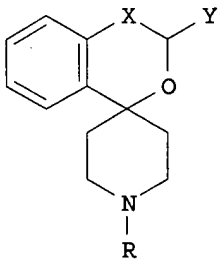
1-(3-(4-((4-Benzylpiperidin-1-yl)methyl)phenoxy)propyl)piperidine **398473-54-6P**, 2-(4-Chlorophenyl)-5-[4-(3-(piperidin-1-yl)propoxy)benzyl]-2,5-diazabicyclo[2.2.1]heptane **398473-55-7P**, 1-(3-((2'-((Piperidin-1-yl)methyl)biphenyl-4-yl)oxy)propyl)piperidine **398473-56-8P**, 1-[1-[4-(3-(Piperidin-1-yl)propoxy)benzyl]piperidin-4-yl]-1,3-dihydrobenzimidazol-2-one **398473-57-9P**, 1-[3-[4-[1-(3-(Piperidin-1-yl)propyl)-1H-pyrrol-2-yl]phenoxy]propyl]piperidine **398473-58-0P**, 1-(3-Phenylpropen-2-yl)-4-[4-(3-(piperidin-1-yl)propoxy)benzyl]piperazine **398473-59-1P**, 1-(3-(3-((4-(Benzylidene)piperidin-1-yl)methyl)phenoxy)propyl)piperidine **398473-60-4P**, 4-(4-Chlorophenyl)-1-[4-(3-(piperidin-1-yl)propoxy)benzyl]piperidin-4-ol **398473-61-5P**, 1-[4-(3-(Piperidin-1-yl)propoxy)benzyl]-4-(3-phenylpropyl)piperidine **398473-62-6P**, 1-[1-[4-(3-(Piperidin-1-yl)propoxy)benzyl]piperidin-4-yl]-1H-benzimidazole **398473-63-7P 398473-64-8P**, 1-[1-[4-(3-(Piperidin-1-yl)propoxy)benzyl]piperidin-4-yl]-2,3-dihydro-1H-indole **398473-65-9P**, 1-Isopropyl-4-[4-(3-(piperidin-1-yl)propoxy)benzyl]piperazine **398473-66-0P**, 1-[4-(3-(Piperidin-1-yl)propoxy)benzyl]azacyclotridecane **398473-67-1P**, 1-Methyl-4-[4-(3-(piperidin-1-yl)propoxy)benzyl]piperazine **398473-68-2P**, 5-Bromo-1-[1-[4-(3-(piperidin-1-yl)propoxy)benzyl]piperidin-4-yl]-2,3-dihydro-1H-indole **398473-69-3P**, 2-[1-[3-(4-((Piperidin-1-yl)methyl)phenoxy)propyl]piperidin-2-yl]ethanol **398473-70-6P**, 4-[3-(4-((Piperidin-1-yl)methyl)phenoxy)propyl]morpholine **398473-71-7P**, 2-[4-(2-(Piperidin-1-yl)ethoxy)benzyl]-1,2,3,4-tetrahydroisoquinoline **398473-72-8P**, 1-[4-(3-(Piperidin-1-yl)propoxy)benzyl]-1,2,3,4-tetrahydroquinoline **398473-73-9P**, 1-[2-(4-((Piperidin-1-yl)methyl)phenoxy)ethyl]piperidine **398473-74-0P**, Dimethyl[3-(4-((piperidin-1-yl)methyl)phenoxy)propyl]amine **398473-75-1P**, 5-(3-(Piperidin-1-yl)propoxy)-2-[4-(3-(piperidin-1-yl)propoxy)phenyl]pyrimidine **398473-76-2P**, 1-Methyl-4-[3-(4-((piperidin-1-yl)methyl)phenoxy)propyl]piperazine **398473-77-3P**, 1-[4-(2-(Piperidin-1-yl)ethoxy)benzyl]-1,2,3,4-tetrahydroquinoline **398473-78-4P**, (4-Chlorophenyl)[3-(3-(piperidin-1-yl)propoxy)benzyl]amine **398473-79-5P**, 1-Benzyl-4-[4-(3-(piperidin-1-yl)propoxy)phenyl]piperidin-4-ol **398473-80-8P**, 1-Isopropyl-4-[4-(3-(piperidin-1-yl)propoxy)phenyl]piperazine **398473-82-0P**, 1-Benzyl-4-[4-(3-(pyrrolidin-1-yl)propoxy)phenyl]piperazine **398473-84-2P**, 1-[4-(3-(Piperidin-1-yl)propoxy)phenyl]piperazine **398473-85-3P**, 1-[4-(3-(Pyrrolidin-1-yl)propoxy)phenyl]piperazine **398473-86-4P**, 1-[3-[2'-(1-Isopropylpiperidin-4-yl)biphenyl-4-yloxy]propyl]piperidine **398473-87-5P**, 1-[3-[4-[2-(1-Methylpyrrolidin-2-yl)ethyl]phenoxy]propyl]piperidine **398473-88-6P**, 1-(3-(4-((1-Isopropylpiperidin-4-yl)methyl)phenoxy)propyl)piperidine **398473-89-7P**, 1-[3-[4-(1-Methylpyrrolidin-2-yl)phenoxy]propyl]piperidine **398473-90-0P**, 1-Isopropyl-4-[4-(3-(piperidin-1-yl)propoxy)phenyl]piperidin-4-ol **398473-91-1P**, [3-(Furan-2-yl)-3-[4-(3-(piperidin-1-yl)propoxy)phenyl]propyl]dimethylamine **398473-92-2P**, 4-[3-[4-(3-(Piperidin-1-yl)propoxy)phenyl]-3-(pyrimidin-2-yl)propyl]morpholine **398473-93-3P**, 4-[4,4,4-Trifluoro-3-[4-(3-(piperidin-1-yl)propoxy)phenyl]butyl]morpholine **398473-94-4P**, (2-(Morpholin-4-yl)ethyl) [4-(3-(piperidin-1-yl)propoxy)phenyl] (pyridin-2-yl)amine **398473-95-5P**, Isopropyl(2-morpholin-4-ylethyl)[4-(3-(piperidin-1-yl)propoxy)phenyl]amine **398473-96-6P**, (2-(Morpholin-4-yl)ethyl)[4-(3-(piperidin-1-yl)propoxy)phenyl]((thiazol-2-yl)methyl)amine **398474-05-0P**, 4-[3-(3-((Piperidin-1-yl)methyl)phenoxy)propyl]morpholine dihydrochloride

398474-06-1P, 1-[3-[4-(2-(Piperidin-1-yl)ethoxy)phenoxy]propyl]piperidine **398474-07-2P**, 1-[3-[4-(3-(Piperidin-1-yl)propoxy)phenoxy]propyl]piperidine **398474-12-9P**, [2-(3-(Piperidin-1-yl)propoxy)benzyl](pyridin-2-yl)amine **398474-13-0P**, (4-Chlorophenyl)[2-(3-(piperidin-1-yl)propoxy)benzyl]amine **398474-14-1P**, 1-[3-[2-((4-(Benzylidene)piperidin-1-yl)methyl)phenoxy]propyl]piperidine **398474-16-3P**, Diethyl[2-(4-((piperidin-1-yl)methyl)phenoxy)ethyl]amine **398474-17-4P**, Diethyl[3-(4-((piperidin-1-yl)methyl)phenoxy)propyl]amine
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug; prepn. of non-imidazole aryloxyalkylamines as **histamine** -H3 receptor antagonists)

IT **398473-97-7P**, 4-[4-(3-Chloropropoxy)phenyl]piperazine-1-carboxylic acid tert-butyl ester **398473-98-8P**, 1-[3-(4-Iodophenoxy)propyl]piperidine **398474-03-8P**, 4'-(3-(Piperidin-1-yl)propoxy)biphenyl-2-carboxaldehyde
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of non-imidazole aryloxyalkylamines as **histamine**-H3 receptor antagonists)

IT **398474-15-2**, Ethyl pyridin-4-yl methylamine
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; prepn. of non-imidazole aryloxyalkylamines as **histamine**-H3 receptor antagonists)

L4 ANSWER 14 OF 36 CA COPYRIGHT 2002 ACS
ACCESSION NUMBER: 136:183692 CA
TITLE: Novel Spiropiperidines as Highly Potent and Subtype Selective .sigma.-Receptor Ligands. Part 1
AUTHOR(S): Maier, Christoph A.; Wuensch, Bernhard
CORPORATE SOURCE: Pharmazeutisches Institut, Universitaet Freiburg, Freiburg i. Br., 79104, Germany
SOURCE: Journal of Medicinal Chemistry (2002), 45(2), 438-448
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB A series of spiro[[2]benzopyran-1,4'-piperidines] and spiro[[2]benzofuran-1,4'-piperidines] of general structure I [X = (CH2)n] is prepd., and the affinity for .sigma.1- and .sigma.2-receptors is investigated by means of

radioligand binding assays. The synthesis of the spiropiperidines, 1'-benzyl-3-methoxy-3,4-dihydrospiro[[2]benzopyran-1,4'-piperidine] (II) and the 1'-benzyl-3-methoxy-3H-spiro[[2]benzofuran-1,4'-piperidine] (III), proceeds via bromine/lithium exchange of the bromoacetals, e.g., 2-(2-bromophenyl)acetaldehyde di-Me acetal in the case of II, addn. to N-benzylpiperidin-4-one, and subsequent cyclization. Systematic variations of the substituent R at the nitrogen atom, the group Y in position 3, and the ring size of the oxygen heterocycle are performed. The .sigma.1- and .sigma.2-receptor affinities are detd. with guinea pig brain and rat liver membrane prepns. using [3H]-labeled (+)-pentazocine and ditolylguanidine, resp. Test results show that a benzyl residue at the piperidine nitrogen atom and a methoxy group in position 3 are advantageous for high .sigma.1-receptor affinity. In this series II and III are among the most potent .sigma.1-ligands interacting in the low nanomolar range with .sigma.1-receptors (14a, Ki = 1.29 nM; 23, Ki = 1.14 nM). Variation of the nitrogen substituent R from benzyl to H, alkyl, Ph, or .omega.-phenylalkyl and the group Y from methoxy to hydroxy, carbonyl, or alkyloxy led to reduced .sigma.1-receptor affinity. In addn. to their high .sigma.1-receptor affinity, the spiropiperidines II and III display excellent selectivity toward .sigma.2-receptors (.sigma.1/.sigma.2 = 2708 and 1130) and several other receptor and reuptake systems. Introduction of a polar hydroxy group in position 3 and elongation of the distance between the piperidine nitrogen atom and the Ph moiety result in ligands with considerable .sigma.2-receptor affinity and therefore diminished .sigma.1/.sigma.2-receptor selectivity. The hemiacetalic 1'-(3-phenylpropyl)-3,4-dihydrospiro[[2]benzopyran-1,4'-piperidin]-3-ol represents the most active .sigma.2-receptor ligand in this series with a Ki value of 83.1 nM.

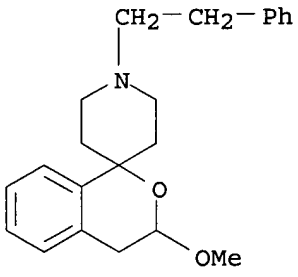
IT **398476-31-8P**

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)

(prepn. and receptor affinity studies of spiropiperidinyl selective .sigma.-receptor ligands via spirocyclization of intermediate hydroxypiperidinylphenylacetaldehyde di-Me acetals)

RN 398476-31-8 CA

CN Spiro[1H-2-benzopyran-1,4'-piperidine], 3,4-dihydro-3-methoxy-1'-(2-phenylethyl)- (9CI) (CA INDEX NAME)



IT **398476-31-8P 398476-34-1P**

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)

(prepn. and receptor affinity studies of spiropiperidinyl selective .sigma.-receptor ligands via spirocyclization of intermediate hydroxypiperidinylphenylacetaldehyde di-Me acetals)

IT **398476-35-2P 398476-36-3P 398476-39-6P 398476-40-9P**

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and receptor affinity studies of spiropiperidinyl selective .sigma.-receptor ligands via spirocyclization of intermediate hydroxypiperidinylphenylacetaldehyde di-Me acetals)

IT **398476-27-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and receptor affinity studies of spiropiperidinyl selective .sigma.-receptor ligands via spirocyclization of intermediate hydroxypiperidinylphenylacetaldehyde di-Me acetals)

IT **398476-32-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and receptor affinity studies of spiropiperidinyl selective .sigma.-receptor ligands via spirocyclization of intermediate hydroxypiperidinylphenylacetaldehyde di-Me acetals)

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 15 OF 36 CA COPYRIGHT 2002 ACS
ACCESSION NUMBER: 136:167581 CA
TITLE: Synthetic studies on glycosphingolipids from Protostomia phyla: synthesis of amphoteric glycolipid analogues containing a phosphocholine residue from the earthworm Pheretima hilgendorfi
AUTHOR(S): Hada, Noriyasu; Sato, Koji; Sakushima, Jun-Ichiro; Goda, Yukihiro; Sugita, Mutsumi; Takeda, Tadahiro
CORPORATE SOURCE: Kyoritsu College of Pharmacy, Tokyo, 105-8512, Japan
SOURCE: Chemical & Pharmaceutical Bulletin (2001), 49(11), 1464-1467
CODEN: CPBTAL; ISSN: 0009-2363
PUBLISHER: Pharmaceutical Society of Japan
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

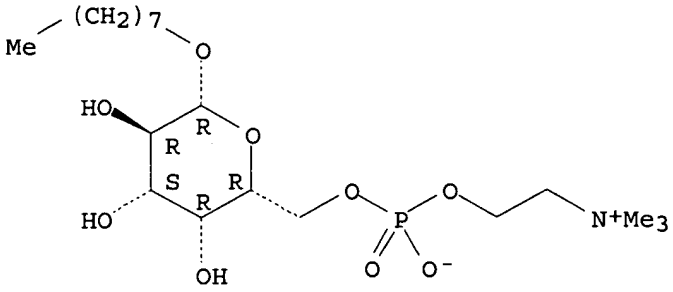
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Two kinds of amphoteric glycosphingolipid analogs from the earthworm Pheretima hilgendorfi were synthesized as follows: The key reaction is a coupling of a phosphocholine group at the position C-6 of the glycoside which was attempted using 2-chloro-2-oxo-1,3,2-dioxaphospholane, followed by reaction of the resulting cyclic phosphate intermediate with anhyd. trimethylamine. Subsequent debenzylation afforded target compds. I and II. Their ability to inhibit the **histamine** release in vitro was examd.

IT **397249-83-1P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and **histamine** release inhibition of amphoteric glycolipid analogs contg. a phosphocholine residue from the earthworm Pheretima hilgendorfi)

RN 397249-83-1 CA
CN .beta.-D-Galactopyranoside, octyl, 6-[2-(trimethylammonio)ethyl hydrogen phosphate], inner salt (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT **397249-83-1P 397249-88-6P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and **histamine** release inhibition of amphoteric glycolipid analogs contg. a phosphocholine residue from the earthworm Pheretima hilgendorfi)

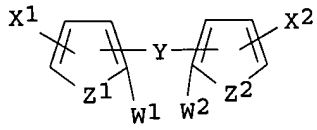
IT **397249-82-0P 397249-87-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and **histamine** release inhibition of amphoteric glycolipid analogs contg. a phosphocholine residue from the earthworm Pheretima hilgendorfi)

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 16 OF 36 CA COPYRIGHT 2002 ACS
ACCESSION NUMBER: 136:167374 CA
TITLE: Preparation of (e.g.) pyrrolylalkylphenyl derivatives as **histamine** H3 antagonists
INVENTOR(S): Bogenstaetter, Michael; Chai, Wenying; Kwok, Annette K.
PATENT ASSIGNEE(S): Ortho McNeil Pharmaceutical, Inc., USA
SOURCE: PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002012224	A2	20020214	WO 2001-US24654	20010806
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002037896	A1	20020328	US 2001-922622	20010806

PRIORITY APPLN. INFO.: US 2000-223768P P 20000808
US 2001-922622 A 20010806
OTHER SOURCE(S): MARPAT 136:167374
GI



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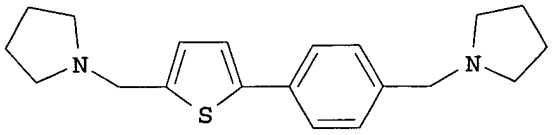


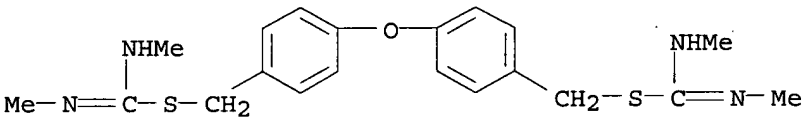
II

AB Title compds. I [X1 = Ga, RaGa, LaGa, RaLaGa; X2= Gb, RbGb, LbGb, RbLbGb; Ga-b= NR3aR4a or NR3bR4b, resp., or pyrrolidinyl, imidazolidinyl, pyrazolidinyl, piperidyl, isoindolinyl, morpholinyl, piperazinyl, imidazolyl, thiazolinyl, 5,6-dihydro-3-imidazo[2,1-b]thiazolyl, thiazolyl; R3a, R4a, R3b, R4b = H, alkyl, cycloalkyl, cycloalkyl-alkyl; Gb can be further selected from NO2, halo, OH, CHO, pyrrolyl, or C(:NOH)H; Ra-b = O, S, NH, C=O; each of La-b = alkylene; Y = covalent bond where one of Z1-2 = N, O, S; Y can also be SO2, C:O, CH2, CH2CH2, OCH2, CH2O, NRc; Rc = H, alkyl, cycloalkyl, cycloalkyl-alkyl, heterocyclyl, heterocyclyl-alkyl, Ph, phenyl-alkyl, or di(alkylamino)-alkyl; Z1-2= N, O, S, CH=CH to form a Ph ring;] were prepd. For instance, 5-formylthiophen-2-ylboronic acid was coupled to 4-bromobenzaldehyde (dioxane, Pd2(dba)3, t-Bu3P, Cs2CO3, 80.degree.C, 24 h) and the product used to reductively alkylate pyrrolidine (CH2Cl2, NaBH(OAc)3, HOAc, 16 h) to give II. II had Ki = 9.0 nM for the **histamine** H3 receptor. I are useful for treating **histamine**-mediated disorders, e.g., narcolepsy, sleep disorders, ADHD, etc.

IT **397871-91-9P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug; prepn. of (e.g.) pyrrolylalkylphenyl derivs. as **histamine** H3 antagonists)

RN 397871-91-9 CA

CN Carbamimidothioic acid, N,N'-dimethyl-, oxybis(4,1-phenylenemethylene) ester (9CI) (CA INDEX NAME)



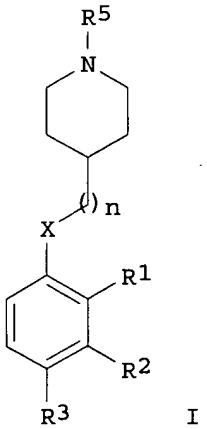
IT **397871-91-9P 397871-92-0P 397871-97-5P**
397872-03-6P 397872-04-7P 397872-06-9P
397872-07-0P 397872-08-1P 397872-21-8P
397872-22-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug; prepn. of (e.g.) pyrrolylalkylphenyl derivs. as **histamine** H3 antagonists)

L4 ANSWER 17 OF 36 CA COPYRIGHT 2002 ACS
ACCESSION NUMBER: 136:167285 CA
TITLE: Preparation of aryloxypiperidines as **histamine** H3 receptor antagonists
INVENTOR(S): Apodaca, Richard; Carruthers, Nicholas I.; Dvorak, Curt A.; Shah, Chandravadan R.; Xiao, Wei
PATENT ASSIGNEE(S): Ortho McNeil Pharmaceutical, Inc., USA
SOURCE: PCT Int. Appl., 155 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002012190	A2	20020214	WO 2001-US24660	20010806
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002040024	A1	20020404	US 2001-922619	20010806

PRIORITY APPLN. INFO.: US 2000-223768P P 20000808
US 2001-922619 A 20010806
OTHER SOURCE(S): MARPAT 136:167285
GI



I

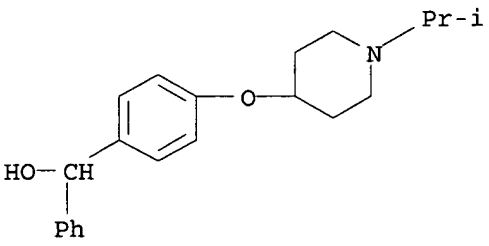
AB Title compds. I [X = O; n = 0-3; R5 = alk(en)yl, cycloalkylalkyl, phenylalk(en)yl, alkylcarbonylalkyl; R1-3 = G, W, wherein one of the remaining two is selected from H and halo and the third being H; G = alk(en/yn)yl-N-contg. heterocycle, etc.; W = CN, CHO, halo, heterocyclyl,

phenoxy, Ph, etc.] were prepd. For example, a suspension of 1-isopropylpiperidin-4-ol (prepn. given), 4-fluorobenzaldehyde and Cs2CO3 were heated to 100.degree. in DMF for 22 h resulting in the formation of 4-[(1-isopropylpiperidin-4-yl)oxy]benzaldehyde (II). II had Ki = 36 nM for the **histamine** H3 receptor. I are useful in the treatment of **histamine**-mediated conditions.

IT **397275-14-8P**, [4-((1-Isopropylpiperidin-4-yl)oxy)phenyl]phenylmethanol
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug; prepn. of aryloxypiperidines as **histamine** H3 receptor antagonists)

RN 397275-14-8 CA

CN Benzenemethanol, 4-[[1-(1-methylethyl)-4-piperidinyl]oxy]-.alpha.-phenyl- (9CI) (CA INDEX NAME)



IT **397275-14-8P**, [4-((1-Isopropylpiperidin-4-yl)oxy)phenyl]phenylmethanol **397275-34-2P**, 4-((1-Isopropylpiperidin-4-yl)oxy)benzaldehyde **397275-61-5P**, 1-[4-((1-Isopropylpiperidin-4-yl)oxy)phenyl]piperazine **397275-85-3P**, [1-[4-((1-Isopropylpiperidin-4-yl)oxy)benzyl]piperidin-4-yl]methanol **397277-24-6P**, 3-((1-Isopropylpiperidin-4-yl)oxy)benzaldehyde
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug; prepn. of aryloxypiperidines as **histamine** H3 receptor antagonists)

IT **397274-77-0P**, 4-(4-(Imidazol-1-yl)phenoxy)-1-isopropylpiperidine **397274-82-7P**, 4-(4-(Imidazol-1-yl)phenoxy)-1-isobutylpiperidine **397274-85-0P**, 1-Isopropyl-4-(4-(pyrrol-1-yl)phenoxy)piperidine **397274-89-4P**, 5-Chloro-2-[4-((1-isopropylpiperidin-4-yl)oxy)phenyl]-1H-benzimidazole **397274-92-9P**, [4-((1-Isopropylpiperidin-4-yl)oxy)phenyl]phenylmethanone **397274-96-3P**, 4-(Biphenyl-4-yloxy)-1-isopropylpiperidine **397275-00-2P**, 4-(4-Benzyloxyphenoxy)-1-isopropylpiperidine **397275-06-8P**, 1-Isopropyl-4-(4-phenoxyphenoxy)piperidine **397275-10-4P**, 1-Isopropyl-4-(4-(Benzyl)phenoxy)piperidine **397275-17-1P**, N-[4-((1-Isopropylpiperidin-4-yl)oxy)phenyl]acetamide **397275-21-7P**, 4-(4-(Cyclopentyl)phenoxy)-1-isopropylpiperidine **397275-30-8P**, 4-((1-sec-Butylpiperidin-4-yl)oxy)benzonitrile **397275-42-2P**, 4-((1-Isopropylpiperidin-4-yl)oxy)benzonitrile **397275-49-9P**, 4-((1-Isobutylpiperidin-4-yl)oxy)benzonitrile **397275-53-5P**, 4-((1-Propylpiperidin-4-yl)oxy)benzonitrile **397275-57-9P**, 1-Isopropyl-4-[4-((1-isopropylpiperidin-4-yl)oxy)phenyl]piperazine **397275-65-9P**, 1-[4-((1-Isopropylpiperidin-4-yl)oxy)benzyl]piperidine **397275-69-3P**, 4-[4-((1-sec-Butylpiperidin-4-yl)oxy)benzyl]morpholine **397275-78-4P**, 1-[4-((1-

Isobutylpiperidin-4-yl)oxy)benzyl]piperidine **397275-81-9P**, 1-n-Isopropyl-4-[4-[5-(1-isopropylpiperidin-4-ylsulfanyl)tetrazol-1-yl]phenoxy]piperidine **397275-89-7P**, 1-[4-((1-Isopropylpiperidin-4-yl)oxy)benzyl]-4-methyl[1,4]diazepane **397275-94-4P**, 1-[4-((1-Isopropylpiperidin-4-yl)oxy)benzyl]azepane **397275-97-7P**, 1-[4-((1-Isopropylpiperidin-4-yl)oxy)benzyl]piperidin-4-ol **397276-01-6P**, [4-((1-Isopropylpiperidin-4-yl)oxy)benzyl]methyl-(1-methylpiperidin-4-yl)amine **397276-05-0P**, 1-[4-((1-Isopropylpiperidin-4-yl)oxy)benzyl]-4-benzylpiperidine **397276-09-4P**, N-[4-((1-Isopropylpiperidin-4-yl)oxy)benzyl]-N,N',N'-trimethylethane-1,2-diamine **397276-13-0P**, 1-[4-((1-Isopropylpiperidin-4-yl)oxy)benzyl]-4-methylpiperazine **397276-17-4P**, Cyclohexyl[4-((1-isopropylpiperidin-4-yl)oxy)benzyl]methylamine **397276-20-9P**, Butyl[4-((1-isopropylpiperidin-4-yl)oxy)benzyl]methylamine **397276-29-8P**, 1-Isopropyl-4-(4-((pyrrolidin-1-yl)methyl)phenoxy)piperidine **397276-33-4P**, Diethyl[4-((1-isopropylpiperidin-4-yl)oxy)benzyl]amine **397276-37-8P**, 1-[4-((1-Isopropylpiperidin-4-yl)oxy)benzyl]-4-phenylpiperazine **397276-45-8P**, 1-Benzyl-4-[4-((1-isopropylpiperidin-4-yl)oxy)benzyl]piperazine **397276-49-2P**, 4-[4-(4-Benzylidenepiperidin-1-ylmethyl)phenoxy]-1-isopropylpiperidine **397276-53-8P**, 4-[4-((1-Isopropylpiperidin-4-yl)oxy)benzyl]morpholine **397276-55-0P**, [4-((1-Isopropylpiperidin-4-yl)oxy)benzyl]dimethylamine **397276-63-0P**, 4-[4-((1-Isobutylpiperidin-4-yl)oxy)benzyl]morpholine **397276-67-4P**, 4-[4-((1-Propylpiperidin-4-yl)oxy)benzyl]morpholine **397276-80-1P**, 4-[4-(4-((Piperidin-1-yl)methyl)phenoxy)piperidin-1-yl]butan-2-one **397276-84-5P**, Cyclopropyl [4-((1-isopropylpiperidin-4-yl)oxy)benzyl] amine **397276-88-9P**, [4-((1-Isopropylpiperidin-4-yl)oxy)benzyl](5-methylpyridin-2-yl)amine **397276-93-6P**, 4-((1-(Isopropyl)piperidin-4-yl)oxy)benzyl pyridin-2-yl amine **397276-98-1P**, [4-((1-Isopropylpiperidin-4-yl)oxy)benzyl] phenyl amine **397277-01-9P**, (5-Chloropyridin-2-yl) [4-((1-isopropylpiperidin-4-yl)oxy)benzyl] amine **397277-07-5P**, 4-[4-(1-(tert-Butoxycarbonyl)piperidin-4-yloxy)phenyl]piperazine-1-carboxylic acid tert-butyl ester **397277-16-6P**, 4-(4-((Morpholin-4-yl)methyl)phenoxy)piperidine-1-carboxylic acid tert-butyl ester **397277-31-5P**, 4-[4-(4-((Morpholin-4-yl)methyl)phenoxy)piperidin-1-yl]butan-2-one **397277-37-1P**, 4-[4-[1-(1-Methylheptyl)piperidin-4-yloxy]benzyl]morpholine **397277-39-3P**, 4-[3-((1-Isopropylpiperidin-4-yl)oxy)benzyl]morpholine **397277-42-8P**, 1-[4-((1-Propylpiperidin-4-yl)oxy)benzyl]piperidine **397277-45-1P**, 1-[4-[1-(1-Methylheptyl)piperidin-4-yloxy]benzyl]piperidine **397277-51-9P**, 4-((1-Ethylpiperidin-4-yl)oxy)benzonitrile **397277-54-2P**, 4-((1-Phenethylpiperidin-4-yl)oxy)benzonitrile **397277-64-4P**, 4-[(1-(2-Hydroxy-1-methylethyl)piperidin-4-yl)oxy]benzonitrile **397277-71-3P 397277-77-9P**, 1-[4-(1-Isopropylpiperidin-4-ylmethoxy)benzyl]piperidine **397277-96-2P**, 4-((1-Isopropylpiperidin-4-yl)oxy)aniline
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug; prepn. of aryloxypiperidines as **histamine** H3 receptor antagonists)

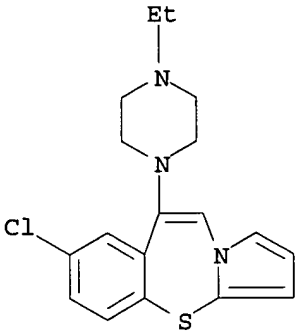
IT **397277-82-6P 397277-85-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of aryloxypiperidines as **histamine** H3 receptor antagonists)

L4 ANSWER 18 OF 36 CA COPYRIGHT 2002 ACS
ACCESSION NUMBER: 136:160868 CA
TITLE: Pyrrolo[1,3]benzothiazepine-Based Atypical Antipsychotic Agents. Synthesis, Structure-Activity Relationship, Molecular Modeling, and Biological Studies
AUTHOR(S): Campiani, Giuseppe; Butini, Stefania; Gemma, Sandra; Nacci, Vito; Fattorusso, Caterina; Catalanotti, Bruno; Giorgi, Gianluca; Cagnotto, Alfredo; Goegan, Mara; Mennini, Tiziana; Minetti, Patrizia; Di Cesare, M. Assunta; Mastroianni, Domenico; Scafetta, Nazzareno; Galletti, Bruno; Stasi, M. Antonietta; Castorina, Massimo; Pacifici, Licia; Ghirardi, Orlando; Tinti, Ornella; Carminati, Paolo
CORPORATE SOURCE: Dipartimento Farmaco Chimico Tecnologico, Universita degli Studi di Siena, Siena, 53100, Italy
SOURCE: Journal of Medicinal Chemistry (2002), 45(2), 344-359
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The prototypical dopamine and serotonin antagonist (.+-.)-7-chloro-9-(4-methylpiperazin-1-yl)-9,10-dihydropyrrolo[2,1-b][1,3]benzothiazepine (5) was resolved into its R and S enantiomers via crystn. of the diastereomeric tartaric acid salts. Binding studies confirmed that the (R)-(-)-enantiomer is a more potent D2 receptor antagonist than the (S)-(+)-enantiomer, with almost identical affinity at the 5-HT2 receptor ((S)-(+)-5, log Y = 4.7; (R)-(-)-5, log Y = 7.4). These data demonstrated a significant stereoselective interaction of 5 at D2 receptors. Furthermore, enantiomer (S)-(+)-5 (ST1460) was tested on a panel of receptors; this compd. showed an intriguing binding profile characterized by high affinity for H1 and the .alpha.1 receptor, a moderate affinity for .alpha.2 and D3 receptors, and low affinity for muscarinic receptors. Pharmacol. and biochem. investigation confirmed an atypical pharmacol. profile for (S)-(+)-5. This atypical antipsychotic lead has low propensity to induce catalepsy in rat. It has minimal effect on serum prolactin levels, and it has been selected for further pharmacol. studies. (S)-(+)-5 increases the extracellular levels of dopamine in the rat striatum after s.c. administration. By use of 5 as the lead compd., a novel series of potential atypical antipsychotics has been developed, some of them being characterized by a stereoselective interaction at D2 receptors. A no. of structure-activity relationships trends have been identified, and a possible explanation is advanced in order to account for the obsd. stereoselectivity of the enantiomer of (.+-.)-5 for D2 receptors. The mol. structure detn. of the enantiomers of 5 by x-ray diffraction and mol. modeling is reported.

IT **395073-83-3P**
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis, structure-activity relationship, mol. modeling, and biol. studies on pyrrolo[1,3]benzothiazepine-based atypical antipsychotic agents)

RN 395073-83-3 CA
CN Pyrrolo[2,1-b][1,3]benzothiazepine, 7-chloro-9-(4-ethyl-1-piperazinyl)-(9CI) (CA INDEX NAME)



IT **395073-83-3P 395073-87-7P 397869-35-1P**
397869-36-2P 397869-38-4P 397869-39-5P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis, structure-activity relationship, mol. modeling, and biol. studies on pyrrolo[1,3]benzothiazepine-based atypical antipsychotic agents)

IT **397869-40-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis, structure-activity relationship, mol. modeling, and biol. studies on pyrrolo[1,3]benzothiazepine-based atypical antipsychotic agents)

REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 19 OF 36 CA COPYRIGHT 2002 ACS
ACCESSION NUMBER: 136:160862 CA
TITLE: Constitutive activity of **histamine** H3 receptors stably expressed in SK-N-MC cells: display of agonism and inverse agonism by H3 antagonists
AUTHOR(S): Wieland, Kerstin; Bongers, Gerold; Yamamoto, Yumiko; Hashimoto, Takeshi; Yamatodani, Atsushi; Menge, Wiro M. B. P.; Timmerman, Henk; Lovenberg, Timothy W.; Leurs, Rob
CORPORATE SOURCE: Leiden/Amsterdam Center for Drug Research, Division of Medicinal Chemistry, Division of Chemistry, Vrije Universiteit, Amsterdam, Neth.
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2001), 299(3), 908-914
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

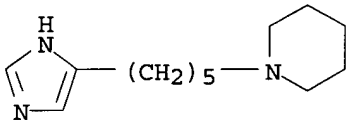
AB Agonist-independent activity of G-protein-coupled receptor, also referred to as constitutive activity, is a well-documented phenomenon and has been reported recently for both the **histamine** H1 and H2 receptors. Using SK-N-MC cell lines stably expressing the human and rat H3 receptors at physiol. receptor densities (500-600 fmol/mg of protein), we show that both the rat and human H3 receptors show a high degree of constitutive activity. The forskolin-mediated cAMP prodn. in SK-N-MC cells is inhibited strongly upon expression of the G1-coupled H3 receptor. The cAMP prodn. can be further inhibited upon agonist stimulation of the H3

receptor and can be enhanced by a variety of H3 antagonists acting as inverse agonists at the H3 receptor. Thioperamide, clobenpropit, and iodophenpropit raise the cAMP levels in SK-N-MC cells with potencies that match their receptor binding affinities. Surprisingly, impentamine and burimamide act as effective H3 agonists. Modification of the amine group of impentamine dramatically affected the pharmacol. activity of the ligand. Receptor affinity was reduced slightly for most impentamine analogs, but the functional activity of the ligands varied from agonist to neutral antagonist and inverse agonist, indicating that subtle changes in the chem. structures of impentamine analogs have major impact on the (de)activation steps of the H3 receptor. In conclusion, upon stable expression of the rat and human H3 receptor in SK-N-MC cells constitutive receptor activity is detected. In this exptl. system, H3 receptors ligands, previously identified as H3 antagonists, cover the whole spectrum of pharmacol. activities, ranging from full inverse agonists to agonists.

IT **397248-38-3**, VUF 5300
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(constitutive activity of **histamine** H3 receptors: display of agonism and inverse agonism by H3 antagonists)

RN 397248-38-3 CA

CN Piperidine, 1-[5-(1H-imidazol-4-yl)pentyl]- (9CI) (CA INDEX NAME)



IT **397248-38-3**, VUF 5300 **397248-39-4**, VUF 5207
397248-40-7, VUF 4904 **397248-41-8**, VUF 4903
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(constitutive activity of **histamine** H3 receptors: display of agonism and inverse agonism by H3 antagonists)

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 20 OF 36 CA COPYRIGHT 2002 ACS

ACCESSION NUMBER: 136:151192 CA

TITLE: Preparation of pyrrolo[2,1-b][1,3]benzothiazepines as antipsychotics.

INVENTOR(S): Minetti, Patrizia; Di Cesare, Assunta; Mastroianni, Domenico; Campiani, Giuseppe; Nacci, Vito

PATENT ASSIGNEE(S): Sigma-Tau Industrie Farmaceutiche Riunite S.p.A., Italy

SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

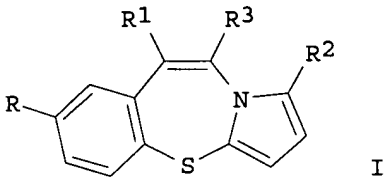
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002010175	A1	20020207	WO 2001-IT406	20010726

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US,

UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: IT 2000-RM432 A 20000801
OTHER SOURCE(S): MARPAT 136:151192
GI

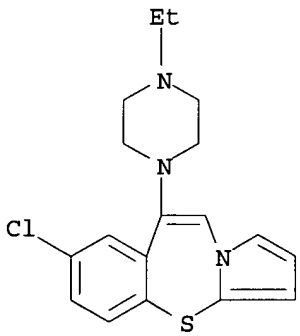


I

AB Title compds. (I; R = H, Cl, Br, F, iodo, alkoxy, alkylthio, alkyl, cycloalkyl; R1 = dialkylamino, 4-alkyl-1-piperazinyl, 4-hydroxyalkyl-1-piperazinyl, 1-imidazolyl, 4-alkyl-1-piperidinyl, 4-alkyl-1-homopiperazinyl; R2 = H, alkoxy, alkylthio, alkyl, CHO, CH=NOH; R3 = H, CHO), were prepd. Thus, 7-chloro-9,10-dihydropyrrolo[2,1-b]benzothiazepin-9-one and N-methylpiperazine were treated with trimethylsilyl trifluoromethanesulfonate followed by heating at 120.degree. for 3 h to give 78% 7-chloro-9-(4-methyl-1-piperazinyl)pyrrolo[2,1-b][1,3]benzothiazepine (ST1508). The latter bound to 5-HT2a, D1, D2, and D3 receptors with Ki = 0.34 nM, 1.9 nM, 0.43 nM, and 2.0 nM, resp.

IT **395073-83-3P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of pyrrolobenzothiazepines as antipsychotics)

RN 395073-83-3 CA
CN Pyrrolo[2,1-b][1,3]benzothiazepine, 7-chloro-9-(4-ethyl-1-piperazinyl)-(9CI) (CA INDEX NAME)



IT **395073-83-3P 395073-87-7P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of pyrrolobenzothiazepines as antipsychotics)

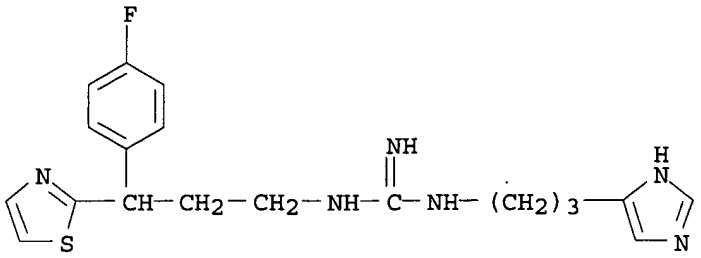
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 21 OF 36 CA COPYRIGHT 2002 ACS
ACCESSION NUMBER: 136:145364 CA
TITLE: Distinct interaction of human and guinea pig **histamine** H2-receptor with guanidine-type agonists
AUTHOR(S): Kelley, Melissa T.; Burckstummer, Tilmann; Wenzel-Seifert, Katharina; Dove, Stefan; Buschauer, Armin; Seifert, Roland
CORPORATE SOURCE: Departments of Pharmacology and Toxicology, The University of Kansas, Lawrence, KS, USA
SOURCE: Molecular Pharmacology (2001), 60(6), 1210-1225
CODEN: MOPMA3; ISSN: 0026-895X
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

AB It is unknown why the potencies and efficacies of long-chained guanidine-type **histamine** H2-receptor (H2R) agonists are lower at the H2R of human neutrophils than at the H2R of the guinea pig atrium. To elucidate these differences, the authors analyzed fusion proteins of the human H2R (hH2R) and guinea pig H2R (gpH2R), resp., and the short splice variant of Gs.alpha. (Gs.alpha.S) expressed in Sf9 cells. The potencies and efficacies of small H2R agonists in the GTPase assay and the potencies of antagonists at inhibiting **histamine**-stimulated GTP hydrolysis by hH2R-Gs.alpha.S and gpH2R-Gs.alpha.S were similar. In contrast, the potencies and efficacies of guanidines were lower at hH2R-Gs.alpha.S than at gpH2R-Gs.alpha.S. Guanidines bound to hH2R-Gs.alpha.S with lower affinity than to gpH2R-Gs.alpha.S, and high-affinity binding of guanidines at gpH2R-Gs.alpha.S was more resistant to disruption by GTP.gamma.S than binding at hH2R-Gs.alpha.S. Mol. modeling suggested that the nonconserved Asp 271 in transmembrane domain 7 of gpH2R (Ala 271 in hH2R) confers high potency to guanidines. This hypothesis was confirmed by Ala 271 .fwdarw. Asp 271 mutation in hH2R-Gs.alpha.S. Intriguingly, the efficacies of guanidines at the Ala 271 .fwdarw. Asp 271 mutant and at hH2R/gpH2R chimeras were lower than at gpH2R. The authors' model suggests that a Tyr 17/Asp 271 H-bond, present only in gpH2R-Gs.alpha.S but not the other constructs studied, stabilizes the active guanidine-H2R state. Collectively, the authors' data show that distinct interaction of H2R species isoforms with guanidines, that a single amino acid in transmembrane domain 7 critically dets. guanidine potency, and that an interaction between transmembrane domains 1 and 7 is important for guanidine efficacy.

IT **391859-94-2**, BU-E 96
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); BIOL (Biological study)
(distinct interaction of human and guinea pig **histamine** H2-receptor with guanidine-type agonists as studied in Sf9 cells in relation to structure activity relationship and pharmacol. properties)

RN 391859-94-2 CA
CN Guanidine, N-[3-(4-fluorophenyl)-3-(2-thiazolyl)propyl]-N'-[3-(1H-imidazol-4-yl)propyl]- (9CI) (CA INDEX NAME)



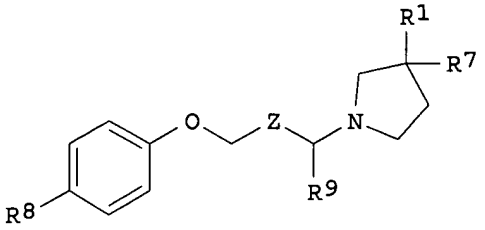
IT **391859-94-2**, BU-E 96 **391859-95-3**, D 281
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); BIOL (Biological study)
(distinct interaction of human and guinea pig **histamine** H2-receptor with guanidine-type agonists as studied in Sf9 cells in relation to structure activity relationship and pharmacol. properties)
REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 22 OF 36 CA COPYRIGHT 2002 ACS
ACCESSION NUMBER: 136:134668 CA
TITLE: Preparation of 1,3-di- and 1,3,3-trisubstituted pyrrolidines as **histamine**-3 receptor ligands for treatment of Alzheimer's disease, ADHD, epilepsy, and narcolepsy
INVENTOR(S): Bennani, Youssef L.; Faghih, Ramin; Dwight, Wesley J.; Vasudevan, Anil; Conner, Scott E.
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: PCT Int. Appl., 146 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

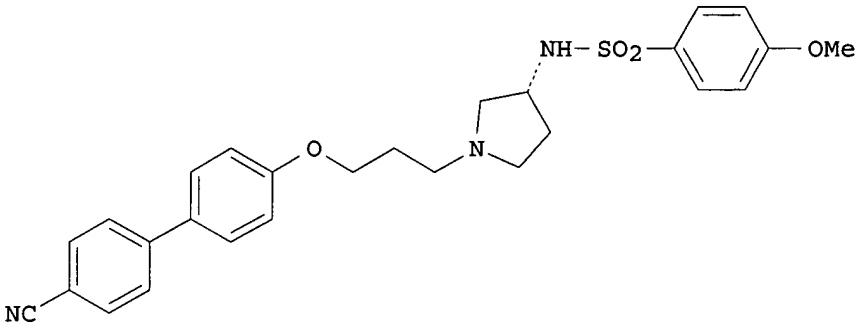
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002006223	A1	20020124	WO 2001-US21929	20010711

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-615151 A 20000713
OTHER SOURCE(S): MARPAT 136:134668
GI



I



II

AB Title compds. I [wherein Z = a bond or CH2; R1 = OR2, NR3R4, or substituted 2,5-dioxoimidazolidinyl; R2 = H, alkoxycarbonyl, alkyl(carbonyl), aminocarbonyl, sulfono, or phosphono; R3 and R4 = independently H, alkenyl(sulfonyl), alkenyl(oxy)carbonyl, alkoxycarbonyl, alkyl(sulfonyl), alkylcarbonyl, aminocarbonyl, aminosulfonyl, alkynyl(sulfonyl), alkynyl(oxy)carbonyl, or (un)substituted (hetero)arylalkyl, (hetero)arylalkenylcarbonyl, etc.; R7 = H or alkyl; or R1 and R7 together form :O; R8 = (cyclo)alkylcarbonyl, or (un)substituted aryl(carbonyl), arylcarbonylaryl, arylcarbonylheterocyclyl, cycloalkylcarbonylaryl, cycloalkylcarbonylheterocyclyl, heterocyclyl(carbonyl), heterocyclylcarbonylaryl, or heterocyclylcarbonylheterocyclyl; R9 = H or alkyl] were prepd. as **histamine**-3 receptor ligands. For example, 4'-[3-[(3R)-3-aminopyrrolidinyl]propoxy][1,1'-biphenyl]-4-carbonitrile in CH2Cl2 was treated with polymer supported N,N-diisopropylethylamine, catalytic N,N-dimethylaminopyridine, and 4-methoxybenzenesulfonyl chloride. After shaking at ambient temp. for 14 h, the mixt. was treated with tris(2-aminoethyl)amine-polystyrene resin and the mixt. shaken for an addnl. 2 h to give the [[(biphenylyloxy)propyl]pyrrolidinyl]benezenesulfon amide II (79%). The latter bound to the **histamine**-3 receptor with Ki of 12 nM. I are useful for the treatment of acute myocardial infarction, asthma, cutaneous carcinoma, depression, inflammation, medullary thyroid carcinoma, melanoma, Meniere's disease, migraine, motion sickness, obesity, pain, Parkinson's disease, schizophrenia, seizures, septic shock, Alzheimer's disease, attention-deficit hyperactivity disorder (ADHD), epilepsy, and narcolepsy.

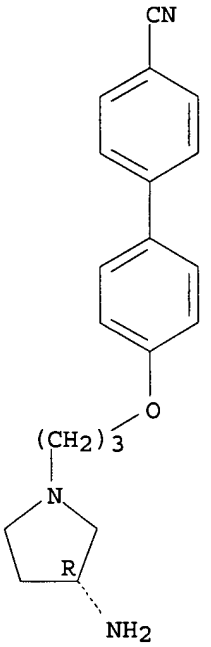
IT **392337-21-2P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(**histamine**-3 receptor ligand; prepn. of di- and trisubstituted pyrrolidines as **histamine**-3 receptor ligands for treatment of Alzheimer's disease, ADHD, epilepsy, and narcolepsy)

RN 392337-21-2 CA

CN [1,1'-Biphenyl]-4-carbonitrile, 4'-[3-[(3R)-3-amino-1-

pyrrolidinyl]propoxy]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **392337-21-2P 392338-14-6P 392338-16-8P**
392338-59-9P 392338-60-2P, 4'-[3-(3-Oxo-1-pyrrolidinyl)propoxy][1,1'-biphenyl]-4-carbonitrile
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(**histamine**-3 receptor ligand; prepn. of di- and trisubstituted pyrrolidines as **histamine**-3 receptor ligands for treatment of Alzheimer's disease, ADHD, epilepsy, and narcolepsy)

IT **392337-05-2P 392337-07-4P 392337-08-5P**
392337-09-6P 392337-10-9P 392337-11-0P
392337-12-1P 392337-13-2P 392337-14-3P
392337-15-4P 392337-16-5P 392337-17-6P
392337-18-7P 392337-19-8P 392337-20-1P
392337-22-3P 392337-23-4P 392337-24-5P
392337-25-6P 392337-26-7P, N-[(3R)-1-[3-[(4'-Cyano[1,1'-biphenyl]-4-yl)oxy]propyl]pyrrolidinyl]-4-methoxybenzenesulfonamide
392337-27-8P 392337-28-9P 392337-29-0P
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392337-33-6P 392337-34-7P 392337-35-8P
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392338-50-0P 392338-51-1P 392338-52-2P
392338-53-3P 392338-54-4P 392338-55-5P
392338-56-6P 392338-57-7P, Cyclopropyl[4-[3-(3-hydroxy-1-pyrrolidinyl)propoxy]phenyl]methanone **392338-58-8P**, Cyclopropyl[4-[3-((3R)-3-hydroxypyrrolidinyl)propoxy]phenyl]methanone **392338-61-3P**, 4'-[3-((3S)-3-Hydroxypyrrolidinyl)propoxy][1,1'-biphenyl]-4-carbonitrile **392338-62-4P**, 4'-[3-(3-Hydroxy-3-methyl-1-pyrrolidinyl)propoxy][1,1'-biphenyl]-4-carbonitrile **392338-63-5P**, 4'-[3-(3-Hydroxy-3-isopropyl-1-pyrrolidinyl)propoxy][1,1'-biphenyl]-4-carbonitrile **392338-64-6P**, 4'-[3-((3R)-3-Hydroxy-3-methylpyrrolidinyl)propoxy][1,1'-biphenyl]-4-carbonitrile
392338-66-8P 392338-67-9P 392338-68-0P
392338-69-1P 392338-71-5P 392338-72-6P
392338-73-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**histamine**-3 receptor ligand; prepn. of di- and trisubstituted pyrrolidines as **histamine**-3 receptor ligands for treatment of Alzheimer's disease, ADHD, epilepsy, and narcolepsy)

IT **392337-06-3P 392338-07-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of di- and trisubstituted pyrrolidines as **histamine**-3 receptor ligands for treatment of Alzheimer's disease, ADHD, epilepsy, and narcolepsy)

IT **392337-91-6 392338-15-7**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; prepn. of di- and trisubstituted pyrrolidines as **histamine**-3 receptor ligands for treatment of Alzheimer's disease, ADHD, epilepsy, and narcolepsy)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

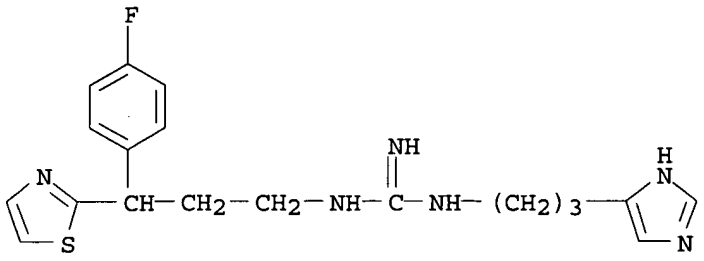
L4 ANSWER 23 OF 36 CA COPYRIGHT 2002 ACS

ACCESSION NUMBER: 136:129344 CA
TITLE: Similar apparent constitutive activity of human **histamine** H2-receptor fused to long and short splice variants of Gs.alpha.
AUTHOR(S): Wenzel-Seifert, Katharina; Kelley, Melissa T.; Buschauer, Armin; Seifert, Roland
CORPORATE SOURCE: Department of Pharmacology and Toxicology, The University of Kansas, Lawrence, KS, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2001), 299(3), 1013-1020
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Fusion proteins allow for the anal. of receptor/G protein coupling under defined conditions. The .beta.2-adrenoceptor (.beta.2AR) fused to the long splice variant of Gs.alpha. (Gs.alpha.L) exhibits a higher apparent constitutive activity than the .beta.2-adrenoceptor fused to the short splice variant of Gs.alpha. (Gs.alpha.S). Exptl., this results in higher efficacy and potency of partial agonists and in higher efficacy of inverse agonists at the .beta.2AR fused to Gs.alpha.L relative to the .beta.2AR fused to Gs.alpha.S, indicating that the agonist-free .beta.2AR and the .beta.2AR occupied by partial agonists promote GDP dissocn. from Gs.alpha.L more efficiently than from Gs.alpha.S. In fact, the GDP affinity of Gs.alpha.S fused to the .beta.2AR is higher than the GDP affinity of Gs.alpha.L fused to the .beta.2AR. We asked the question whether the **histamine** H2-receptor (H2R) exhibits similar coupling to Gs.alpha. splice variants as the .beta.2AR. To address this question, we studied H2R-Gs.alpha. fusion proteins expressed in Sf9 cells. In contrast to .beta.2AR-Gs.alpha. fusion proteins, the potencies and efficacies of partial agonists and the efficacies of inverse agonists were similar at the H2R fused to Gs.alpha.L and Gs.alpha.S as assessed by guanosine-5'-O-(3-thio)triphosphate binding and/or steady-state GTPase activity. However, the time course anal. of guanosine-5'-O-(3-thio)triphosphate binding indicated that Gs.alpha.S fused to the H2R possesses a higher GDP-affinity than Gs.alpha.L fused to the H2R. Our data show that the H2R fused to Gs.alpha.L and Gs.alpha.S possesses similar constitutive activity and is insensitive to differences in GDP affinity of Gs.alpha. splice variants. Thus, GDP affinity of G proteins does not generally det. constitutive activity of receptors.

IT **391859-94-2**, BU-E 96
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); BIOL (Biological study)
(human **histamine** H2-receptor fused to long and short splice variants of Gs.alpha. with potencies and efficacies of partial agonists and efficacies of inverse agonists thereof)

RN 391859-94-2 CA
CN Guanidine, N-[3-(4-fluorophenyl)-3-(2-thiazolyl)propyl]-N'-[3-(1H-imidazol-4-yl)propyl]- (9CI) (CA INDEX NAME)

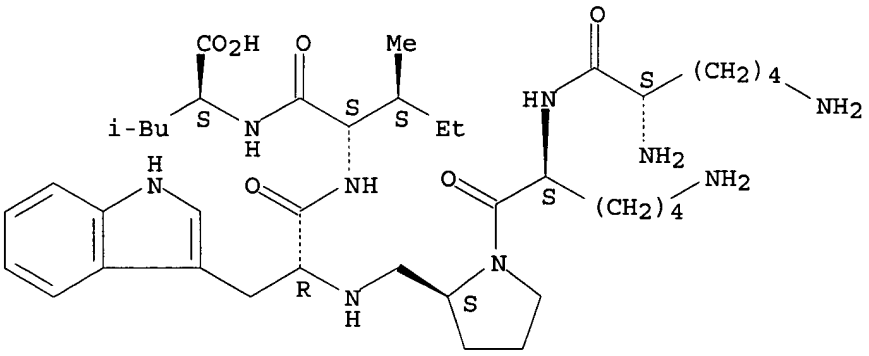


IT **391859-94-2**, BU-E 96 **391859-95-3**, D 281
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); BIOL (Biological study)
(human **histamine** H2-receptor fused to long and short splice variants of Gs.alpha. with potencies and efficacies of partial agonists and efficacies of inverse agonists thereof)
REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 24 OF 36 CA COPYRIGHT 2002 ACS
ACCESSION NUMBER: 136:129284 CA
TITLE: Agonism, inverse agonism, and neutral antagonism at the constitutively active human neurotensin receptor 2
AUTHOR(S): Richard, Francoise; Barroso, Severine; Martinez, Jean; Labbe-Jullie, Catherine; Kitabgi, Patrick
CORPORATE SOURCE: Institut de Pharmacologie Moleculaire et Cellulaire, Centre National de la Recherche Scientifique (CNRS) Unite Mixte Recherche 6097, Valbonne, Fr.
SOURCE: Molecular Pharmacology (2001), 60(6), 1392-1398
CODEN: MOPMA3; ISSN: 0026-895X
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Two G protein-coupled neurotensin (NT) receptors, termed NTR1 and NTR2, have been identified so far. In contrast to the NTR1, which has been extensively studied, little is known about the pharmacol. and biol. properties of the NTR2. In the course of characterizing NT analogs that exhibited binding selectivity for the NTR2, the authors discovered that this receptor constitutively activated inositol phosphate (IP) prodn. Here, the authors report on the constitutive activity of the human NTR2 (hNTR2) transfected in COS cells and on compds. that exhibit agonism, inverse agonism, and neutral antagonism at this receptor. IP levels increased linearly with time, whereas they remained const. in mock-transfected cells. Furthermore, IP prodn. was proportional to the amt. of hNTR2 present at the cell membrane. SR 48692, a nonpeptide antagonist of the NTR1, stimulated IP prodn., whereas levocabastine, a nonpeptide **histamine** H1 antagonist that binds the NTR2 but not the NTR1, behaved as a weak partial inverse agonist. NT analogs modified at position 11 of the NT mol., in particular by the introduction of bulky arom. D amino acids, exhibited binding selectivity at the hNTR2 and also behaved as partial inverse agonists, reversing constitutive IP prodn. up to 50%. Finally, NT barely affected constitutive IP prodn. but antagonized the effects of both agonist and inverse agonist compds., thus behaving as a neutral antagonist. The unique pharmacol. profile of the hNTR2 is discussed in the light of its sequence similarity with the NTR1 and the known binding site topol. of NT and SR 48692 in the NTR1.
IT **392664-51-6**, JMV 2004

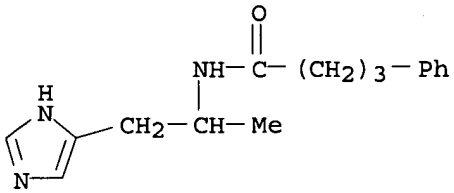
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); BIOL (Biological study)
(agonism, inverse agonism and neutral antagonism at constitutively active human neurotensin receptor 2 transfected in COS cells)
RN 392664-51-6 CA
CN L-Leucine, L-lysyl-L-lysyl-L-prolyl-.psi.-(CH2-NH)-D-tryptophyl-L-isoleucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **392664-51-6**, JMV 2004
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); BIOL (Biological study)
(agonism, inverse agonism and neutral antagonism at constitutively active human neurotensin receptor 2 transfected in COS cells)
REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 25 OF 36 CA COPYRIGHT 2002 ACS
ACCESSION NUMBER: 136:128590 CA
TITLE: QSAR studies on acylated **histamine** derivatives
AUTHOR(S): Agrawal, Vijay K.; Khadikar, Padmakar V.
CORPORATE SOURCE: Department of Chemistry, A. P. S. University, Rewa, 486 003, India
SOURCE: Bioorganic & Medicinal Chemistry (2001), 9(11), 2787-2792
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB H3-receptor antagonists activity in terms of -log Ki for a series of acylated **histamine** derivs. was modeled using topol. indexes, namely negentropy (N), mol. redundancy (MRI), and valence connectivity index (mxv) indexes. Excellent results were obtained in multiple regression anal. upon the introduction of a dummy parameter (indicator parameter). Consistent increase in RA2 value indicated that in spite of obsd. collinearity the proposed models are significant.
IT **391900-64-4**
RL: PAC (Pharmacological activity); PRP (Properties); BIOL (Biological study)
(QSAR studies on acylated **histamine** derivs.)
RN 391900-64-4 CA
CN Benzenebutanamide, N-[2-(1H-imidazol-4-yl)-1-methylethyl]- (9CI) (CA INDEX NAME)



IT **391900-64-4**
RL: PAC (Pharmacological activity); PRP (Properties); BIOL (Biological study)
(QSAR studies on acylated **histamine** derivs.)
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 26 OF 36 CA COPYRIGHT 2002 ACS
ACCESSION NUMBER: 136:123598 CA
TITLE: Production and use of novel peptide-based agents for use with bi-specific antibodies
INVENTOR(S): Hansen, Hans J.; Griffiths, Gary L.; Leung, Shui-on; McBride, William J.; Qu, Zhengxing
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 37 pp., Cont.-in-part of U. S. Ser. No. 337,756.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 14
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002006379	A1	20020117	US 2001-823746	20010403

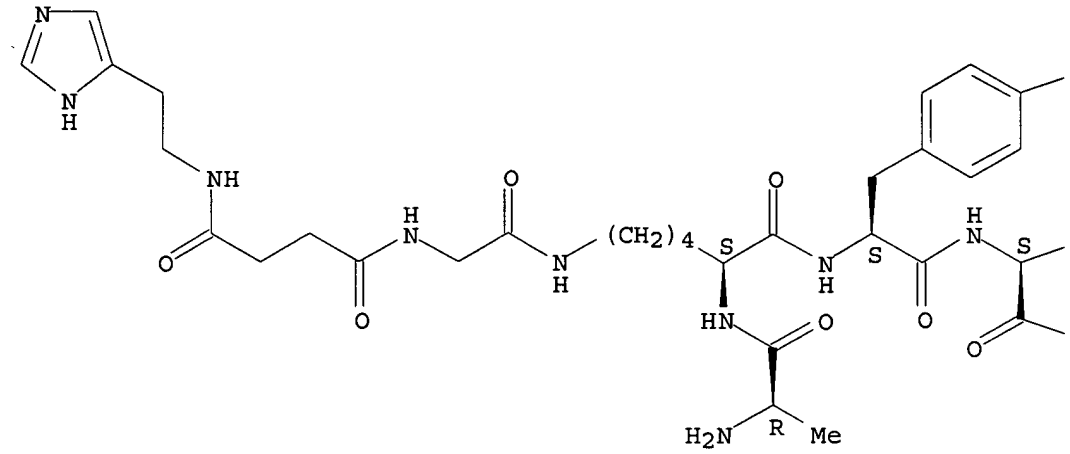
PRIORITY APPLN. INFO.: US 1998-90142P P 19980622
US 1998-104156P P 19981014
US 1999-337756 A2 19990622

AB The present invention relates to a bi-specific antibody or antibody fragment having at least one arm that is reactive against a targeted tissue and at least one other arm that is reactive against a linker moiety. The linker moiety encompasses a hapten to which antibodies have been prepd. The antigenic linker is conjugated to one or more therapeutic or diagnostic agents or enzymes. The invention provides constructs and methods for producing the bispecific antibodies or antibody fragments, as well as methods for using them.

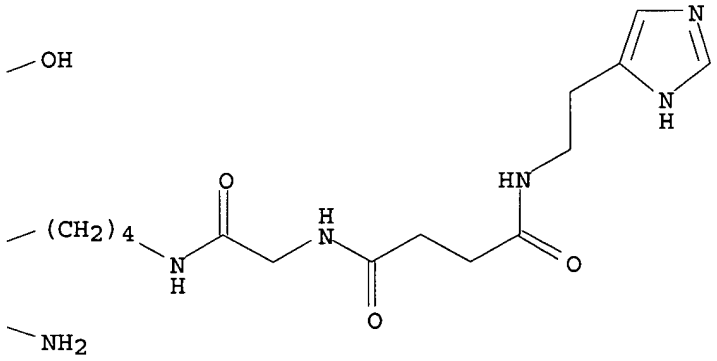
IT **389617-27-0DP**, triazacyclononanetriacetic acid thiol-contg. conjugates
RL: DGN (Diagnostic use); PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(peptide-based diagnostic and therapeutic agents for use with bi-specific antibodies)
RN 389617-27-0 CA
CN L-Lysinamide, D-alanyl-N6-[N-[4-[[2-(1H-imidazol-4-yl)ethyl]amino]-1,4-dioxobutyl]glycyl]-L-lysyl-L-tyrosyl-N6-[N-[4-[[2-(1H-imidazol-4-yl)ethyl]amino]-1,4-dioxobutyl]glycyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



IT **389617-27-0DP**, triazacyclononanetriacetic acid thiol-contg. conjugates **389617-29-2DP**, triazacyclononanetriacetic acid thiol-contg. conjugates
RL: DGN (Diagnostic use); PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(peptide-based diagnostic and therapeutic agents for use with bi-specific antibodies)

IT **391267-27-9P**, IMP 241 **391267-28-0P**, IMP 237 **391267-29-1P**, IMP 243
RL: DGN (Diagnostic use); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(peptide-based diagnostic and therapeutic agents for use with bi-specific antibodies)

L4 ANSWER 27 OF 36 CA COPYRIGHT 2002 ACS
ACCESSION NUMBER: 136:112383 CA
TITLE: **Histamine** H1-receptor activation of nuclear factor-.kappa.B: roles for G.beta..gamma.- and G.alpha.q/11-subunits in constitutive and

agonist-mediated signaling

AUTHOR(S): Bakker, Remko A.; Schoonus, Stefan B. J.; Smit, Martine J.; Timmerman, Henk; Leurs, Rob

CORPORATE SOURCE: Leiden/Amsterdam Center for Drug Research, Department of Pharmacochemistry, Vrije Universiteit Amsterdam, Amsterdam, Neth.

SOURCE: Molecular Pharmacology (2001), 60(5), 1133-1142
CODEN: MOPMA3; ISSN: 0026-895X

PUBLISHER: American Society for Pharmacology and Experimental Therapeutics

DOCUMENT TYPE: Journal

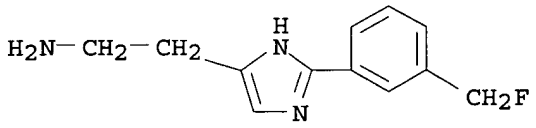
LANGUAGE: English

AB Nuclear factor .kappa.B (NF-.kappa.B) is an important transcription factor in inflammation that has obtained a great interest as a drug target for the treatment of various allergic conditions. In this study, we show that the **histamine** H1 receptor, which is also an important player in allergic and inflammatory conditions, activates NF-.kappa.B in both a constitutive and agonist-dependent manner. Moreover, the obsd. constitutive NF-.kappa.B activation is inhibited by various H1-receptor antagonists, suggesting that inverse agonism may account, at least in part, for their ascribed antiallergic properties. Investigation of the H1 receptor-mediated NF-.kappa.B activation in transfected COS-7 cells indicates that the level of the obsd. constitutive activity of the H1 receptor can be modulated by the expression levels of either G.alpha.-proteins or G.beta..gamma.-heterodimers. Members of the G.alpha.q/11-family of G.alpha.-proteins are most effective in increasing H1 constitutive activity. Also, co-expression of G.beta.2 in combination with either G.gamma.1 or G.gamma.2 results in an increased constitutive activity of the H1 receptor, whereas scavenging of G.beta..gamma.-subunits by co-expression of G.alpha.1 completely neutralizes the constitutive, but not the agonist-induced, NF-.kappa.B activity. Our data suggest that both G.alpha.q/11- and G.beta..gamma.-subunits play a role in the agonist-induced, H1 receptor-mediated NF-.kappa.B activation, but that constitutive NF-.kappa.B activation by the H1 receptor is primarily mediated through G.beta..gamma.-subunits.

IT **390809-59-3**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(roles for G.beta..gamma.- and G.alpha.q/11--subunits in constitutive and agonist-mediated signaling in **histamine** H1-receptor activation of NF-.kappa.B)

RN 390809-59-3 CA

CN 1H-Imidazole-4-ethanamine, 2-[3-(fluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



IT **390809-59-3**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(roles for G.beta..gamma.- and G.alpha.q/11--subunits in constitutive and agonist-mediated signaling in **histamine** H1-receptor activation of NF-.kappa.B)

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 28 OF 36 CA COPYRIGHT 2002 ACS

ACCESSION NUMBER: 136:102616 CA
TITLE: The MOX/SUC precursor strategies: robust ways to construct functionalized oligonucleotides
AUTHOR(S): Polushin, N.
CORPORATE SOURCE: Fidelity Systems, Inc., Gaithersburg, MD, USA
SOURCE: Nucleosides, Nucleotides & Nucleic Acids (2001), 20(4-7), 973-976
CODEN: NNNAFY; ISSN: 1525-7770
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

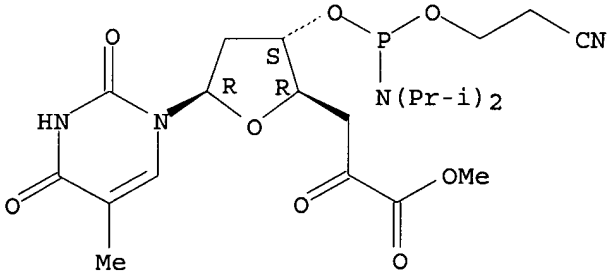
AB The use of phosphoramidites bearing one or more methoxyoxalamido (MOX) or succinimido (SUC) reactive groups for construction of functionalized oligonucleotides is described. The efficiency of the new precursor strategy was demonstrated in the synthesis of oligonucleotide contg. up to 16 imidazole residues.

IT **389088-02-2**
RL: RCT (Reactant); RACT (Reactant or reagent)
(methoxyoxalamido and succinimido precursor strategies provide robust ways to construct functionalized oligonucleotides)

RN 389088-02-2 CA

CN 2-Furanpropanoic acid, 3-[[[bis(1-methylethyl)amino](2-cyanoethoxy)phosphino]oxy]-5-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)tetrahydro-.alpha.-oxo-, methyl ester, (2R,3S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **389088-02-2 389088-03-3 389088-04-4**
389088-05-5 389088-06-6 389088-23-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(methoxyoxalamido and succinimido precursor strategies provide robust ways to construct functionalized oligonucleotides)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 29 OF 36 CA COPYRIGHT 2002 ACS
ACCESSION NUMBER: 136:102398 CA
TITLE: Preparation of 4-amino-2-anilino-5-cyanopyrimidines as antitumor agents
INVENTOR(S): Thomas, Andrew Peter; Newcombe, Nicholas John; Heaton, David William
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 88 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002004429	A1	20020117	WO 2001-GB3084	20010706

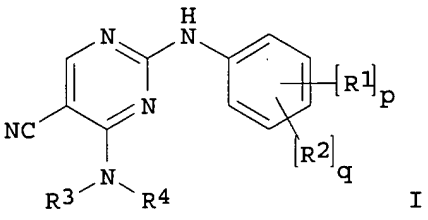
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2000-16877 A 20000711

OTHER SOURCE(S): MARPAT 136:102398

GI



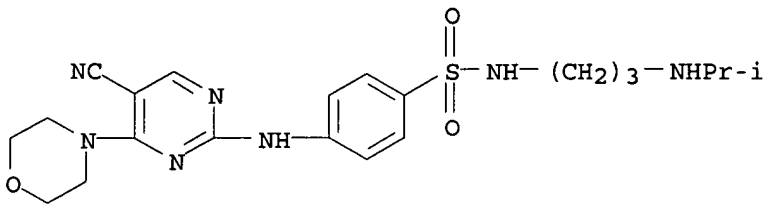
I

AB The title compds. [I; R1 = halo, NO2, CN, etc.; p = 0-4; R2 = sulfamoyl, EB; q = 0-2; p + q = 1-5; R3 = H, alkyl, alkenyl, etc.; R4 = alkyl, alkenyl, alkynyl, etc.; or NR3R4 = (un)substituted heterocyclyl such morpholino; B = alkyl, alkenyl, Ph, etc.; E = CO, NHCO, CONH, etc.], useful as medicaments, particularly medicaments for producing a cell cycle inhibitory (anti-cell-proliferation) effect in a warm-blooded animal, such as man, were prepd. Thus, reacting 2-chloro-5-cyano-4-morpholinopyrimidine with 4-[N-(3-isopropylaminopropyl)sulfamoyl]aniline in the presence of 1N HCl in 2-butanol afforded 19% I [R2 = 4-[N-(3-isopropylaminopropyl)sulfamoyl]; R1 = H; NR3R4 = morpholino] which showed IC50 of 0.148 .mu.M against CDK2. The title compds. I showed IC50's in the range 1.mu.M to 1 nM when tested in assay measuring inhibition of cell growth.

IT **389604-29-9P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 4-amino-2-anilino-5-cyanopyrimidines as antitumor agents)

RN 389604-29-9 CA

CN Benzenesulfonamide, 4-[[5-cyano-4-(4-morpholinyl)-2-pyrimidinyl]amino]-N-[3-[(1-methylethyl)amino]propyl]- (9CI) (CA INDEX NAME)



IT **389604-29-9P 389604-30-2P 389604-31-3P**
389604-32-4P 389604-33-5P 389604-34-6P
389604-35-7P 389604-36-8P 389604-37-9P
389604-38-0P 389604-39-1P 389604-40-4P
389604-41-5P 389604-42-6P 389604-43-7P
389604-44-8P 389604-45-9P 389604-46-0P
389604-47-1P 389604-49-3P 389604-51-7P
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389604-59-5P 389604-60-8P 389604-61-9P
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389604-93-7P 389604-98-2P 389604-99-3P
389605-00-9P 389605-01-0P 389605-02-1P
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389605-09-8P 389605-10-1P 389605-11-2P
389605-12-3P 389605-13-4P 389605-14-5P
389605-15-6P 389605-16-7P 389605-17-8P
389605-18-9P 389605-19-0P 389605-20-3P
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389605-51-0P 389605-52-1P 389605-53-2P
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389605-65-6P 389605-67-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 4-amino-2-anilino-5-cyanopyrimidines as antitumor agents)

IT **389606-64-8 389606-67-1 389606-69-3**
389606-71-7 389606-73-9 389606-75-1
389606-76-2 389606-77-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of 4-amino-2-anilino-5-cyanopyrimidines as antitumor agents)

IT **389605-68-9P 389605-70-3P 389605-71-4P**

389605-72-5P 389605-73-6P 389605-74-7P
389605-75-8P 389605-76-9P 389605-77-0P
389605-78-1P 389605-79-2P 389605-80-5P
389605-81-6P 389605-82-7P 389605-83-8P
389605-84-9P 389605-85-0P 389605-86-1P
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RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of 4-amino-2-anilino-5-cyanopyrimidines as antitumor agents)
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

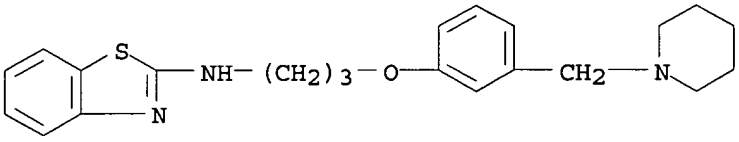
L4 ANSWER 30 OF 36 CA COPYRIGHT 2002 ACS
ACCESSION NUMBER: 136:96459 CA
TITLE: **Histamine** H3-receptor antagonism improves memory retention and reverses the cognitive deficit induced by scopolamine in a two-trial place recognition task
AUTHOR(S): Orsetti, Marco; Ghi, Piera; Di Carlo, Giovanni
CORPORATE SOURCE: Dipartimento di Scienze C.A.F. e Farmacologiche, Universita del Piemonte Orientale, Novara, Italy
SOURCE: Behavioural Brain Research (2001), 124(2), 235-242
CODEN: BBREDI; ISSN: 0166-4328
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Several reports have indicated that, under different exptl. conditions, the administration of **histamine** H3-receptor antagonists exerts procognitive effects by activating central **histaminergic** transmission. In the present study the action of thioperamide, a H3-receptor blocker, is investigated on consolidation and recall mechanisms of the rat place recognition memory. The animals have been tested on a two-trial delayed comparison paradigm in a Y-maze. Thioperamide enhances the memory retention when administered i.p. post-acquisition (0.7 and 5.0 mg/kg are ineffective, whereas the dose of 2.0 mg/kg improves memory) but does not affect the rat performance when injected 45 min prior to the testing trial. The post-acquisition effect

of thioperamide is time-dependent since the administration of the drug 30 min after the end of the training trial has no effect on memory. In addn., thioperamide reverses the amnesia induced by the post-acquisition treatment with 0.02 mg/kg i.p. of scopolamine (SCOP). The procognitive effect of thioperamide is not modified by the contemporary administration of pyrilamine, an **histamine** H1-receptor antagonist. On the contrary, the blockade of H2-receptors by zolantidine 10 mg/kg reverses both the effect of thioperamide alone and the drug action on the scopolamine-induced memory deficit. The results indicate that the neuronal **histamine** released in consequence of the post-acquisition thioperamide treatment improves place recognition memory through the activation of postsynaptic H2-receptors.

IT **388111-69-1**, Zolantidine hydrochloride
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**histamine** H3-receptor antagonism improves memory retention and reverses cognitive deficit induced by scopolamine in a two-trial place recognition task)

RN 388111-69-1 CA

CN 2-Benzothiazolamine, N-[3-[3-(1-piperidinylmethyl)phenoxy]propyl]-, monohydrochloride (9CI) (CA INDEX NAME)



IT **388111-69-1**, Zolantidine hydrochloride
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**histamine** H3-receptor antagonism improves memory retention and reverses cognitive deficit induced by scopolamine in a two-trial place recognition task)

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 31 OF 36 CA COPYRIGHT 2002 ACS
ACCESSION NUMBER: 136:96074 CA
TITLE: Prevention and treatment of degenerative diseases by glutathione and phase II detoxification enzymes
INVENTOR(S): Zhang, Yueshen; Ho, Tony; Li, Yun
PATENT ASSIGNEE(S): Johns Hopkins School of Medicine, USA
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002002190	A2	20020110	WO 2001-US21225	20010705

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,

LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

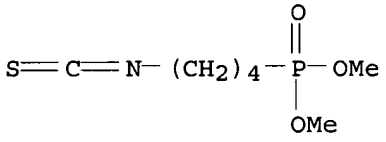
PRIORITY APPLN. INFO.: US 2000-215812P P 20000705

AB The present invention generally relates to the field of treating degenerative disease by administering a pharmaceutically effective amt. of a compd. that elevates glutathione or at least one Phase II detoxification enzyme in diseased tissue. The present invention also relates to a pharmaceutical compn. useful for the treatment of degenerative diseases, as well as a method of identifying agents that modulate intracellular levels of glutathione or intracellular levels of at least one Phase II enzyme in neuronal cells.

IT **387816-42-4**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prevention and treatment of degenerative diseases by glutathione and phase II detoxification enzymes)

RN 387816-42-4 CA

CN Phosphonic acid, (4-isothiocyanatobutyl)-, dimethyl ester (9CI) (CA INDEX NAME)



IT **387816-42-4**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prevention and treatment of degenerative diseases by glutathione and phase II detoxification enzymes)

L4 ANSWER 32 OF 36 CA COPYRIGHT 2002 ACS

ACCESSION NUMBER: 136:95912 CA

TITLE: NF449: a subnanomolar potency antagonist at recombinant rat P2X1 receptors

AUTHOR(S): Braun, Kirsten; Rettinger, Jurgen; Ganso, Matthias; Kassack, Matthias; Hildebrandt, Caren; Ullmann, Heiko; Nickel, Peter; Schmalzing, Gunther; Lambrecht, Gunter

CORPORATE SOURCE: Biocentre Niederursel, Department of Pharmacology, University of Frankfurt, Frankfurt/Main, 60439, Germany

SOURCE: Naunyn-Schmiedeberg's Archives of Pharmacology (2001), 364(3), 285-290
CODEN: NSAPCC; ISSN: 0028-1298

PUBLISHER: Springer-Verlag

DOCUMENT TYPE: Journal

LANGUAGE: English

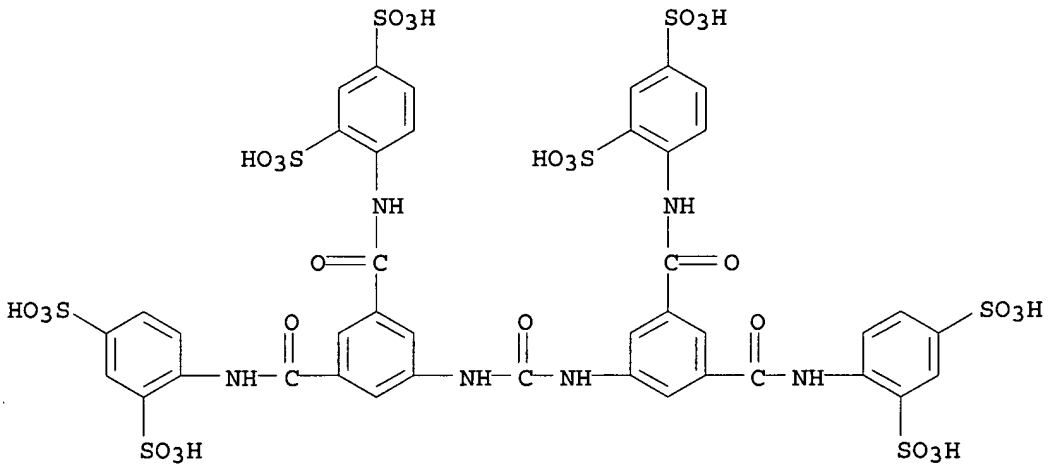
AB Antagonistic effects of the novel suramin analog 4,4',4'',4'''-(carbonylbis(imino-5,1,3-benzenetriylbis(carbonylimino)))tetrakis-benzene-1,3-disulfonic acid (NF449) were studied on contractions of the rat vas deferens elicited by .alpha.,.beta.-methylene ATP (.alpha..beta.meATP; mediated by P2X1 receptors), contractions of the guinea-pig ileal longitudinal smooth muscle elicited by .alpha..beta.meATP (mediated by P2X3 receptors) or adenosine 5'-O-(2-thiodiphosphate) (ADP.beta.S;

mediated by P2Y1 receptors), ATP-induced increases of [Ca2+]i in human embryonic kidney (HEK) 293 cells (mediated by P2Y2 receptors), inward currents evoked by ATP in follicle cell-free Xenopus laevis oocytes expressing rP2X1 or rP2X3 receptors and degrdn. of ATP by ecto-nucleotidases in folliculated Xenopus laevis oocytes. In addn., NF449 was examd. for its P2 receptor specificity in rat vas deferens (.alpha.1A-adrenoceptors) and guinea-pig ileum (**histamine** H1 and muscarinic M3 receptors).At native (pIC50=7.15) and recombinant (pIC50=9.54) P2X1 receptors, NF449 was a highly potent antagonist. The P2X3 receptors present in guinea-pig ileum (pIC50=5.04) or expressed in oocytes (pIC50.apprxeq.5.6) were much less sensitive for NF449. It also was a very weak antagonist at P2Y1 receptors in guinea-pig ileum (pIC50=4.85) and P2Y2 receptors in HEK 293 cells (pIC50=3.86), and showed very low inhibitory potency on ecto-nucleotidases (pIC50<3.5). NF449 (100 .mu.M) did not interact with .alpha.1A-adrenoceptors or **histamine** H1 and muscarinic M3 receptors. Thus, the antagonism by NF449 is highly specific for P2 receptors. In conclusion, the subnanomolar potency at rP2X1 receptors and the rank order of potency, P2X1 >> P2X3 > P2Y1 > P2Y2 > ecto-nucleotidases, make NF449 unique among the P2 receptor antagonists reported to date. NF449 may fill the long-standing need for a P2X1-selective radioligand.

IT **389142-38-5**, NF 449
RL: PAC (Pharmacological activity); BIOL (Biological study)
(NF449 as a subnanomolar potency antagonist at recombinant rat P2X1 receptors)

RN 389142-38-5 CA

CN 1,3-Benzenedisulfonic acid, 4,4',4'',4'''-[carbonylbis[imino-5,1,3-benzenetriylbis(carbonylimino)]]tetrakis- (9CI) (CA INDEX NAME)

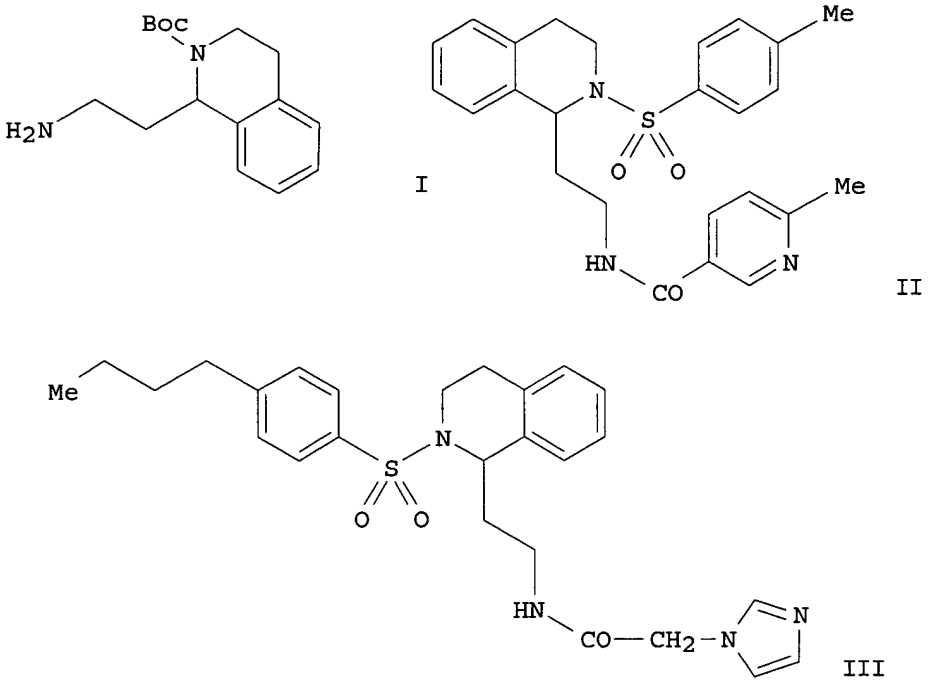


IT **389142-38-5**, NF 449
RL: PAC (Pharmacological activity); BIOL (Biological study)
(NF449 as a subnanomolar potency antagonist at recombinant rat P2X1 receptors)

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 33 OF 36 CA COPYRIGHT 2002 ACS
ACCESSION NUMBER: 136:95568 CA
TITLE: Parallel synthesis and biological activity of a new class of high affinity and selective .delta.-opioid ligand

AUTHOR(S): Barn, D. R.; Caulfield, W. L.; Cottney, J.; McGurk, K.; Morphy, J. R.; Rankovic, Z.; Roberts, B.
CORPORATE SOURCE: Organon Laboratories Ltd., Newhouse, ML1 5SH, UK
SOURCE: Bioorganic & Medicinal Chemistry (2001), 9(10), 2609-2624
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



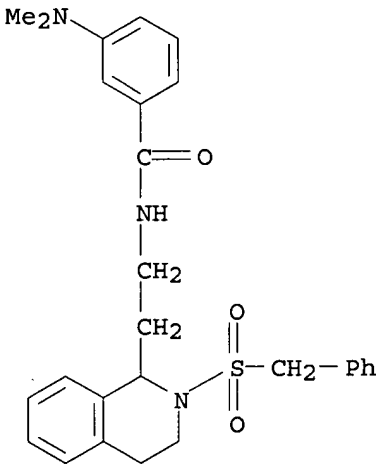
AB A considerable no. of research papers describing the synthesis and testing of the delta opioid receptor (DOR) ligands, SNC-80 and TAN-67, and analogs of these two compds., have been published in recent years. However, there have been few reports of the discovery of completely new structural classes of selective DOR ligand. By optimizing a hit compd. identified by high throughput screening, a new series of tetrahydroisoquinoline sulfonamide-based delta opioid ligands was discovered. The main challenge in this series was to simultaneously improve both affinity and physicochem. properties, notably aq. soly. The most active ligand had an affinity (IC50) of 6 nM for the cloned human DOR, representing a 15-fold improvement relative to the original hit I (IC50 98 nM). Compds. from this new series show good selectivity for the DOR over .mu. and .kappa. opioid receptors. However the most active and selective compds. had poor aq. soly. Improved aq. soly. was obtained by replacing the phthalimide group in I by basic groups, allowing the synthesis of salt forms. A series of compds. with improved affinity and soly. relative to I was identified and these compds. showed activity in an in vivo model of antinociception, the formalin paw test. In the case of compd. II, this analgesic activity was shown to be mediated primarily via a DOR mechanism.

The most active compd. in vivo, III, showed superior potency in this test compared to the ref. DOR ligand, TAN-67 and similar potency to morphine (68% and 58% inhibition in Phases 1 and 2, resp., at a dose of 10 mmol/kg i.v.).

IT **388626-03-7P**
RL: CPN (Combinatorial preparation); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses)
(dparallel synthesis and biol. activity of a new class of high affinity and selective .delta.-opioid ligand)

RN 388626-03-7 CA

CN Benzamide, 3-(dimethylamino)-N-[2-[1,2,3,4-tetrahydro-2-[(phenylmethyl)sulfonyl]-1-isoquinolinyl]ethyl]- (9CI) (CA INDEX NAME)



IT **388626-03-7P**
RL: CPN (Combinatorial preparation); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses)
(dparallel synthesis and biol. activity of a new class of high affinity and selective .delta.-opioid ligand)

IT **388626-30-0P 388627-87-0P 388628-83-9P**
RL: CPN (Combinatorial preparation); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses)
(eparallel synthesis and biol. activity of a new class of high affinity and selective .delta.-opioid ligand)

IT **388626-94-6P**
RL: CPN (Combinatorial preparation); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses)
(lparallel synthesis and biol. activity of a new class of high affinity and selective .delta.-opioid ligand)

IT **388629-20-7P**
RL: CPN (Combinatorial preparation); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses)
(nparallel synthesis and biol. activity of a new class of high affinity and selective .delta.-opioid ligand)

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RL: CPN (Combinatorial preparation); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses)
(parallel synthesis and biol. activity of a new class of high affinity and selective .delta.-opioid ligand)

IT **388629-21-8P 388629-22-9P 388629-23-0P**
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RL: CPN (Combinatorial preparation); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses)
(parallel synthesis and biol. activity of a new class of high affinity and selective .delta.-opioid ligand)

IT **388625-50-1P 388625-51-2P 388625-52-3P**
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RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(parallel synthesis and biol. activity of a new class of high affinity and selective .delta.-opioid ligand)
IT **388629-95-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(parallel synthesis and biol. activity of a new class of high affinity and selective .delta.-opioid ligand)
IT **388625-46-5P 388625-48-7P 388625-49-8P 388629-96-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(parallel synthesis and biol. activity of a new class of high affinity and selective .delta.-opioid ligand)
REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 34 OF 36 CA COPYRIGHT 2002 ACS
ACCESSION NUMBER: 136:84706 CA
TITLE: Identification and characterization of (Na,K) ATPase CD3 domain as **histamine**-releasing factor (HRF) receptor and HRF-binding peptides used as **histamine**-releasing inhibitors in allergy treatment
INVENTOR(S): Lee, Kyunglim; Chung, Junho; Kim, Wha Jung; Kim, Miyoung; Jung, Jaehoon
PATENT ASSIGNEE(S): S. Korea
SOURCE: Eur. Pat. Appl., 81 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1167526	A1	20020102	EP 2001-113424	20010601

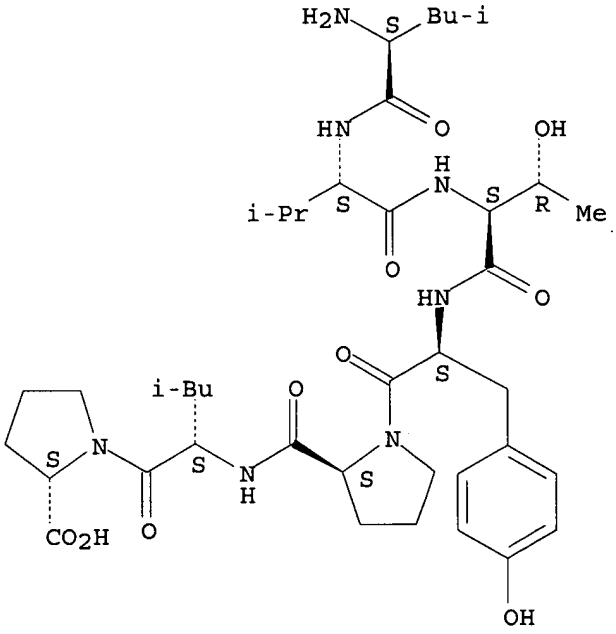
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
PRIORITY APPLN. INFO.: KR 2000-30130 A 20000601
AB Disclosed are IgE-dependent **histamine**-releasing factor (HRF) receptor, HRF-binding peptides and nucleic acids encoding the same, and uses thereof in the medicinal area. Specifically, The invention provides protein and cDNA sequences for novel **histamine**-releasing factor (HRF) receptors which are the third cytoplasmic domains (CD3) of (Na,K) ATPase .alpha. subunits (.alpha.1, .alpha.2 and .alpha.3) from human and rat identified by yeast two-hybrid assay and confocal microscope. The invention reveals the mechanism by HRF stimulates **histamine** release from basophils by repressing the (Na,K) ATPase activity and increasing intracellular Na+ and Ca2+ concns. through activating Na+/Ca2+ exchanger. Further, in the presence of IgE, intracellular Ca2+ is further increased due to the generation of ROS, which ultimately stimulates **histamine** release. The invention also provides HRF receptor expression vector, recombinant host cells and methods for drug screening and diagnosis and therapy of allergies. Moreover, the invention provides peptides (with the formula:(A, L or W)-X-X-X-X-(A, L, S or W)-(A, P or M), wherein X represents any amino acid), which inhibit **histamine** release by binding to HRF with a high specific affinity.
IT **385384-11-2**
RL: PRP (Properties)
(unclaimed sequence; identification and characterization of (Na,K) ATPase CD3 domain as **histamine**-releasing factor (HRF)

receptor and HRF-binding peptides used as **histamine**-releasing inhibitors in allergy treatment)

RN 385384-11-2 CA

CN L-Proline, L-leucyl-L-valyl-L-threonyl-L-tyrosyl-L-prolyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **385384-11-2 385384-12-3 385384-13-4**
385384-14-5 385384-15-6 385384-16-7
385384-17-8 385384-18-9 385384-19-0
385384-20-3
RL: PRP (Properties)
(unclaimed sequence; identification and characterization of (Na,K) ATPase CD3 domain as **histamine**-releasing factor (HRF) receptor and HRF-binding peptides used as **histamine**-releasing inhibitors in allergy treatment)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 35 OF 36 CA COPYRIGHT 2002 ACS

ACCESSION NUMBER: 136:84446 CA

TITLE: Peptide-based analysis of amino acid sequences important to the biological activity of eosinophil granule major basic protein

AUTHOR(S): Thomas, L. L.; Kubo, H.; Loegering, D. J.; Spillard, K.; Weaver, A. J.; McCormick, D. J.; Weiler, C.; Gleich, G. J.

CORPORATE SOURCE: Department of Immunology/Microbiology, Rush Medical College, Chicago, IL, 60612, USA

SOURCE: Immunology Letters (2001), 78(3), 175-181
CODEN: IMLED6; ISSN: 0165-2478

PUBLISHER: Elsevier Science Ireland Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Synthetic peptides corresponding to amino acid sequences in eosinophil

granule major basic protein (MBP) were evaluated for cytotoxic activity toward K562 cells and for ability to stimulate basophil mediator release. Results obtained using 14 peptides spanning the 117-amino acid sequence of MBP in overlapping fashion indicated that the activities mapped to peptide sequences near the amino and carboxy termini of MBP. The activity of these regions was confirmed using two peptides corresponding to MBP residues 18-45 and 89-117. A 20-h incubation with 5 .mu.M peptide 18-45 or peptide 89-117 caused approx. the same levels (>60%) of cytotoxicity in K562 cells as 5 .mu.M MBP. Similarly, a 30-min incubation with peptides 18-44 and 89-117 stimulated basophil **histamine** release in a concn.-dependent manner over the range of 5-20 .mu.M. The level of release stimulated by 20 .mu.M peptide 89-117 approached that stimulated by 2 .mu.M MBP. A 20 .mu.M concn. of peptide 89-117 also stimulated leukotriene C4 (LTC4) prodn. by the basophils. Neither peptide 18-45 nor peptide 89-117 was cytotoxic for basophils under the exptl. conditions for **histamine** and LTC4 release, as detd. by 51Cr release. These results indicate that two MBP peptide sequences, including one (89-117) that contains a unique carbohydrate-binding region, share the biol. activities of MBP.

IT **386210-85-1**

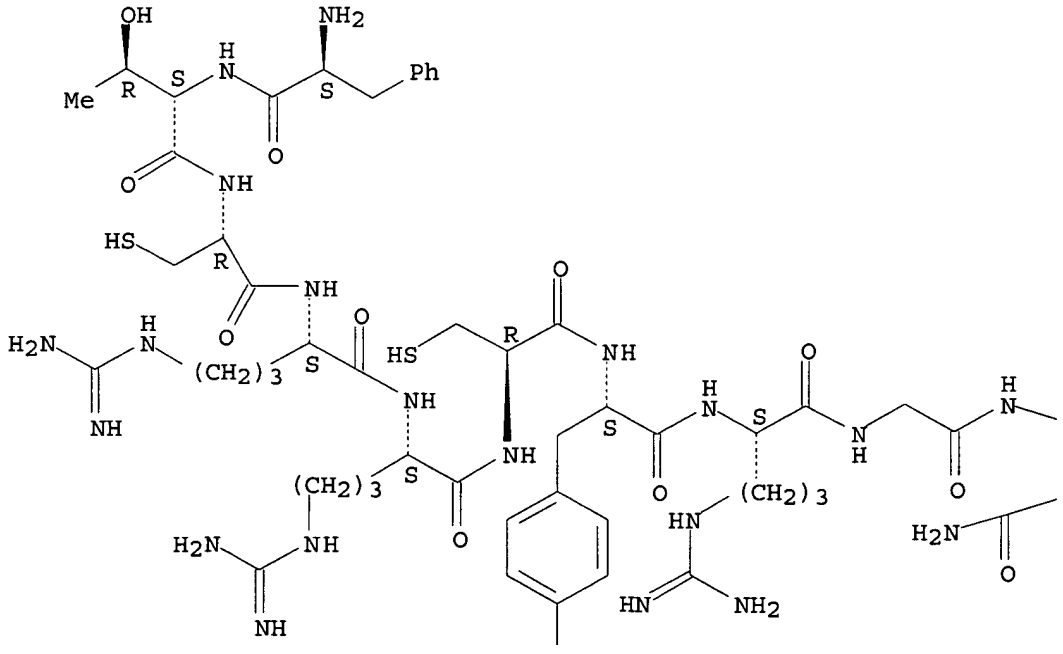
RL: BSU (Biological study, unclassified); BIOL (Biological study) (peptide-based anal. of amino acid sequences important to biol. activity of eosinophil granule major basic protein)

RN 386210-85-1 CA

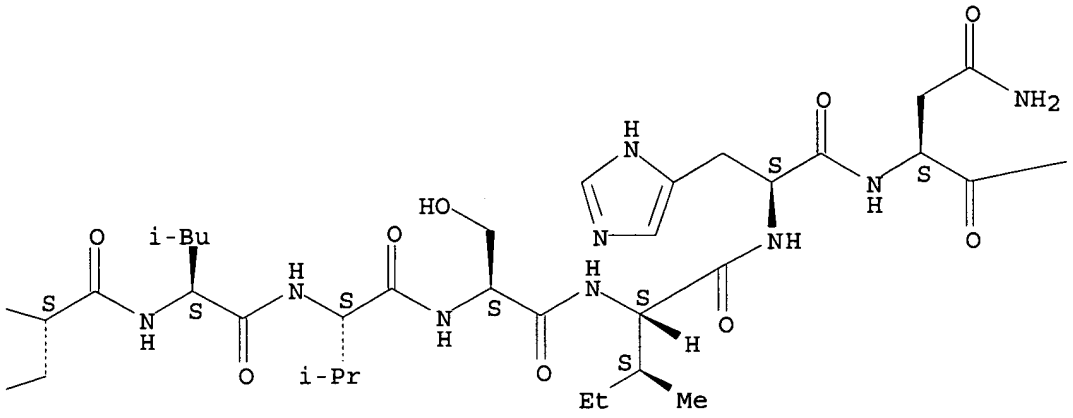
CN L-Serine, L-phenylalanyl-L-threonyl-L-cysteinyl-L-arginyl-L-arginyl-L-cysteinyl-L-tyrosyl-L-arginylglycyl-L-asparaginyl-L-leucyl-L-valyl-L-seryl-L-isoleucyl-L-histidyl-L-asparaginyl-L-phenylalanyl-L-asparaginyl-L-isoleucyl-L-asparaginyl-L-tyrosyl-L-arginyl-L-isoleucyl-L-glutaminyl-L-cysteinyl-L-seryl-L-valyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



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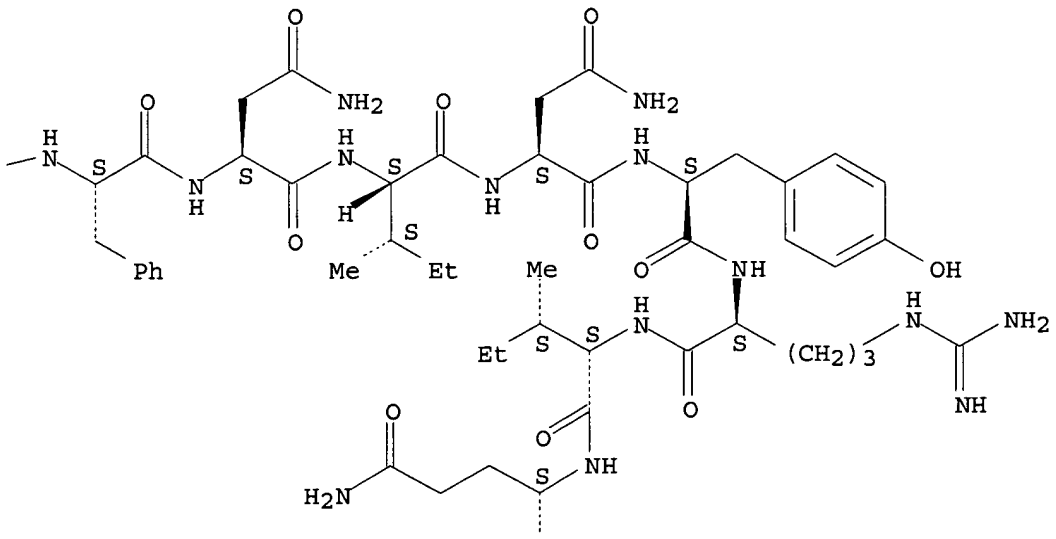
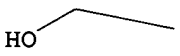


PAGE 2-A

PAGE 2-B



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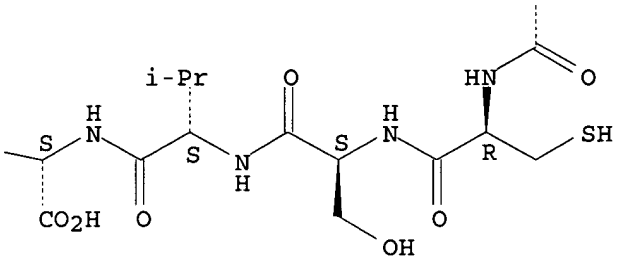


IT **386210-85-1 386210-86-2**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(peptide-based anal. of amino acid sequences important to biol. activity of eosinophil granule major basic protein)
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 36 OF 36 CA COPYRIGHT 2002 ACS
ACCESSION NUMBER: 136:78970 CA
TITLE: System zones in capillary zone electrophoresis
AUTHOR(S): Beckers, Jozef L.; Gebauer, Petr; Bocek, Petr
CORPORATE SOURCE: Department of Chemistry (SPO), Eindhoven University of Technology, Eindhoven, Neth.
SOURCE: Electrophoresis (2001), 22(17), 3648-3658
CODEN: ELCTDN; ISSN: 0173-0835
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English

AB This paper brings an overview of system zones (SZs) in capillary zone electrophoresis (CZE) and their effects upon the migration of zones of analytes. The formation and migration of SZs is an inherent feature of CZE, and it depends predominantly on the compn. of an actual background electrolyte (BGE). One can distinguish between stationary SZs and migrating SZs. Stationary SZs, which move due to the electroosmotic flow only, are induced in any BGE by sample injection. Migrating SZs may be induced by a sample injection in BGEs which show at least one of the following features: (i) BGE contains two or more co-ions, (ii) BGE has low or high pH whereby H+ or OH- act as the 2nd co-ion, and (iii) BGE contains multivalent weak acids or bases. SZs do not contain any analyte and show always BGE-like compn. They contain components of the BGE only and the concns. of these components are different from their values in the original BGE. Providing that some of the ionic components of the BGE are visible by the detector, the migrating SZs can be detected and they are present as system peaks/dips in the electropherogram. A migrating SZ may be characterized by its mobility, and examples are given how this mobility can depend on the compn. of the BGE. Further, the effects of the

migrating SZs (either visible or not visible by the detector) upon the zones of analytes are presented and the typical disturbances of the peaks (extra broadening, zigzag form, schizophrenic behavior) are exemplified and discussed. Finally, some conclusions are presented how to cope with the SZs in practice. The proposed procedure is based on the theor. predictions and/or measurements of the mobilities of SZs and on the so-called unsafe region. Then, such operational conditions should be selected where the unsafe region is outside of the required anal. window.

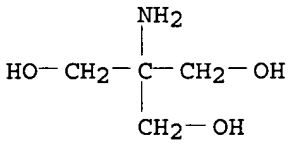
IT **384329-92-4**, Tris formate
RL: ARU (Analytical role, unclassified); PRP (Properties); ANST (Analytical study)
(in study of system zones capillary zone electrophoresis)

RN 384329-92-4 CA

CN Formic acid, compd. with 2-amino-2-(hydroxymethyl)-1,3-propanediol (1:1) (9CI) (CA INDEX NAME)

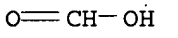
CM 1

CRN 77-86-1
CMF C4 H11 N O3



CM 2

CRN 64-18-6
CMF C H2 O2



IT **384329-92-4**, Tris formate **384329-93-5**, Tris maleate
384329-94-6, Tris butyrate **384329-95-7**
384329-96-8, Tris phthalate **384329-97-9**,
Histamine acetate **384331-33-3**, Tris caproate
384331-34-4, Tris caprylate
RL: ARU (Analytical role, unclassified); PRP (Properties); ANST (Analytical study)
(in study of system zones capillary zone electrophoresis)

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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